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The American Heart Journal

VOL. IV DECEMBER, 1928 No. 2

Original Communications

THE TREATMENT OF RHEUMATIC CARDITIS BY ROENTGEN IRRADIATION OF THE HEART*

ROBERT L. LEVY, M.D., AND ROSS GOLDEN, M.D.
NEW YORK, N. Y.

INTRODUCTION

THERE are reasons for believing that roentgen rays, in suitable doses, might be expected to exercise an effect upon rheumatic lesions in the heart. Roentgen therapy has been successfully employed in the treatment of certain low grade infections, such as tuberculous lymphadenitis, acne, and iritis. Even more acute inflammatory conditions, such as carbuncles, furuncles, and erysipelas are often favorably influenced. The result of treatment appears to be a modification of the local tissue reaction, but the mechanism by which this is brought about is not understood.

Another effect of roentgen therapy is its effect upon scar tissue. Cicatrices of the skin become softer and more flexible after irradiation and keloids may be greatly reduced in size. In undertaking the present work, the treatment was at first given with the idea of modifying the character of the tissues in the region of the mitral valve in cases of mitral stenosis. In order to avoid any possibility of injury to the heart, small doses were used, comparable to those employed in the treatment of local infections. As it became apparent that changes were being induced in the myocardium with these quantities of irradiation, larger amounts were not employed. The amount of irradiation necesary to modify scar tissue is greater than such dosage and the time required for the change to occur is relatively long. It is probable, therefore, that this effect played no rôle in the results now reported.

LITERATURE

A detailed review of the literature concerning the effects of roentgen irradiation on the cardiovascular system was given in an earlier

*From the Department of Medicine, College of Physicians and Surgeons of Columbia University and the Presbyterian Hospital.

Read at the Meeting of the Association of American Physicians, Washington, D. C., June 2, 1928.

paper.[1] In summary, it has been shown that roentgen-ray therapy, though recommended for the relief of certain types of cardiac pain, is of doubtful value.[2] Post-mortem examination of the heart of one patient with Hodgkin's disease who received irradiation over the mediastinum showed myocardial lesions believed to denote specific roentgen-ray injury to the heart muscle.[3] In numerous other patients receiving roentgen therapy over the chest for various forms of thoracic tumor, and examined electrocardiographically and at necropsy, no evidence of cardiac damage was found.[4] In a series of rabbits irradiated over the heart with doses comparable to those employed in the clinic, transitory ventricular premature beats were recorded once. Pathologically, no characteristic changes were noted.[5] Following exposure of the right lung of dogs to considerably larger doses, cell necrosis, hemorrhage, and proliferation of connective tissue were found in the musculature of the right auricle.[6]

Since this abstract of previous work was compiled, three papers have appeared dealing with this subject. Tsuzuki[7] irradiated rabbits through the back. Thirty-six hours after exposure to 24 per cent of the skin erythema dose, he found fatty granules in the heart muscle cells. After 32 per cent of the erythema dose was given, the muscle cells showed beginning fatty degeneration; this was more distinct at the end of ninety-six hours. The author was uncertain whether the changes described were due to the direct or indirect effect of the rays.

Hartman and his collaborators[8] irradiated the anterior thoracic wall of dogs and sheep with from 3 to 18 times the human erythema dose given either in a single, massive exposure or in repeated smaller applications. Following such treatment they found gross and microscopic lesions in the heart muscle, and alterations in the electrocardiographic records. The graphic changes reported were inversion of the T-waves and the appearance of abnormal forms of T; cardiac irregularities, such as paroxysmal tachycardia, auricular flutter, and fibrillation; slight prolongation of the P-R interval; diminished voltage of QRS. It must be borne in mind that the amount of rays used was many times greater than is ever employed for clinical purposes. These authors also present the records of three patients who were given relatively large amounts of irradiation over the cardiac area incidental to treatment for mediastinal or lung tumors. Necropsy was performed in each instance and microscopic changes were described in the myocardium comparable to those found in the experimental animals. These reports do not present convincing evidence as to the relation between roentgen therapy and the changes observed in the heart. As stated by the authors, terminal infection in two cases and the advanced age of the third patient probably had a bearing on the findings.

Warthin and Pohle[9] exposed the precordium of rats and rabbits to a single dose of roentgen rays of short wave-length, the surface dose

being equivalent to one human erythema dose. No clinical symptoms of roentgen-ray injury were noted and there were no gross pathological changes at necropsy. In one out of twenty-four rabbits an unusual degree of Zenker's necrosis was found on microscopic examination. In two of thirty rats, hyaline degeneration was found in the heart muscle, of a degree warranting the conclusion that this change was caused by irradiation. It was concluded that a single exposure of the precordium of these animals to the dose described did not produce definite and irreparable injury to the heart.

MATERIAL AND METHOD OF STUDY

Two reports of our work have already been made.[1] In the present paper, further observations are included and a more detailed clinical analysis has been undertaken. Thirty patients with rheumatic carditis have received roentgen irradiation to the heart with the idea of attempting to influence the cardiac lesions of rheumatism in a favorable manner. In the group are included cases exhibiting various phases of rheumatic infection—acute and chronic, febrile and afebrile. There were patients in the first attack with early cardiac involvement; others had large hearts, severely damaged valves, and advanced mechanical defects. In seven cases, paroxysms of heart pain were a dominant feature. The material was intentionally varied in order to learn, if possible, which types of rheumatic heart disease might be affected by irradiation. In addition to noting changes in clinical condition, frequent electrocardiograms and numerous teleroentgenograms were made.

TECHNIC OF IRRADIATION

With the aid of a cross-section diagram of the chest at the level of the fourth chondrosternal junction and a depth-dose chart, there was calculated a quantity of rays yielding about 10 per cent of the erythema dose throughout the region of the heart. This was given in two fields, both front and back, large enough to include the entire cardiac area, each field being centered about 5 cm. to the left of the midline. It seemed advisable to use small doses in order to avoid any possible injury to the heart and because the quantity of rays used in the treatment of infections is not large.

The machine setting was: 200 KV (peak); 50 cm. target skin distance; 0.5 mm. copper plus 1.0 mm. aluminum filter. The usual dose was 36 milliampere minutes over the front and 54 to 72 milliampere minutes over the back, depending upon the size of the chest. If nausea and vomiting occurred, subsequent doses were decreased to 8 per cent of the calculated erythema dose. The treatment was repeated every two weeks until four had been given. At least a month was allowed to elapse before undertaking another series. The number of irradiations given to one patient ranged from two to twenty-five; most patients received at least one series of four. In this group of cases, it appeared likely that at least one series of four treatments was necessary to initiate improvement, when this occurred. More prolonged therapy is probably desirable. Modification of the technic may yield better results.

RESULTS

Changes in the Electrocardiogram.—In normal individuals, the form of the electrocardiogram remains quite constant over long periods of time. As a result of disease of the heart, changes may occur. In rheumatic fever, electrocardiographic evidence of myocardial involvement, as shown by alterations in the form of the graphs, is frequently obtainable.[10] These changes are not to be regarded as specific for rheumatism; they are merely an expression of disturbance in the heart

TABLE I

SUMMARY

30 Cases
249 Roentgen Irradiations
649 Electrocardiograms

DURATION OF FOLLOW-UP SINCE FIRST IRRADIATION	
3 years	3 cases
2 to 3 years	4 cases
1 to 2 years	9 cases
Less than 1 year	14 cases
ELECTROCARDIOGRAPHIC CHANGES	
Present	17 cases
Absent	13 cases
CLINICAL CONDITION	
Improved at the End of the Follow-Up Period	21 cases
Improved Temporarily	3 cases
Unimproved	1 case
Died	5 cases
RELATIONSHIP OF ELECTROCARDIOGRAPHIC CHANGES TO CLINICAL CONDITION	
Improvement with EKG. Changes	14 cases
Improvement without EKG. Changes	10 cases
EKG. Changes without Improvement	3 cases
Neither Improvement nor EKG. Changes	3 cases

muscle. In this study, several control records were always made and the effect of digitalis was excluded. Except for occasional shortening of A-V conduction time,[11] salicylates, in our experience, do not modify the electrocardiogram in rheumatic fever. It is believed that the changes observed in our cases were due to the effect of irradiation on rheumatic lesions in the heart muscle. The fact that changes in the form of the graphs did not occur in every instance lends support to the concept; for myocardial lesions are not found in every case of rheumatic heart disease. Furthermore, it seems probable that the lesions vary in their susceptibility to the effects of irradiation at different stages of their evolution. It is impossible at present to form an opinion concerning the possible effect of the rays on valvular lesions.

Changes in the form of the electrocardiogram were observed in 17 of the 30 cases. In 14 of these 17 cases, clinical improvement was also noted. But clinical improvement was noted also in 10 cases in which no graphic changes were recorded. It appears, then, that change in clinical condition and change in the electrocardiogram do not necessarily parallel each other; but following irradiation, electrocardiographic change without betterment is uncommon.

The alterations in the form of the curves were of numerous varieties:

a. Inversion or deepening of the T-waves—18 cases. This was the change most frequently observed. It was seen sometimes in all leads, but occasionally only in Lead III. In Fig. 1 is shown an example of this effect. Slight deepening of the T-wave in Lead III is seen on the day following the first exposure (May 28). Six weeks after beginning roentgenotherapy, and after the fourth treatment, T_3 is seen to be sharply inverted and T_2 distinctly flattened (July 9). Treatments were then discontinued. By December 29, some five months later, T_3 was upright and T_2 higher. Following a second series of roentgen-ray exposures, the T-waves again showed changes similar to those seen after the first series, though of somewhat less marked degree. The same sequence of events was repeated a third time. In this case, clinical improvement was striking.

b. Inversion or flattening of the P-wave—9 cases. This was seen as a transitory change, appearing usually soon after beginning roentgenotherapy and, as in the case of the T-wave changes, sometimes recurring after successive courses.

c. Change in electrical axis—7 cases. This was an interesting finding. It is a change which we have observed also in cases of rheumatic heart disease with active myocardial lesions, uninfluenced by roentgenotherapy. The shift was always in the direction of right axis deviation. (Fig. 2.)

d. Change in the form of QRS—5 cases. Variations in the position and shape of the notch in R or S, as well as differences in the duration of QRS were noted. In the example pictured in Fig. 3, changes in the form and direction of P and T are also shown.

e. Ventricular premature beats—3 cases. These occurred within a day or two after exposure and suggested the possibility of an irritative reaction in the myocardium (Fig. 1).

f. Auricular premature beats—2 cases. These probably have the same significance as the extrasystoles of ventricular origin.

g. Elevation or depression of the R-T interval—2 cases. Like the other changes, this denotes disturbance in the myocardium.

h. Shortening of auriculo-ventricular conduction time—1 case. (See Table II.)

Table II

L. V., Male, Aged Sixteen. Presbyterian Hospital No. 64000

Date	Radio-therapy	EKG. Data						Attacks of pain in 24 hr.	Highest temp.	Salicylate (gm.) daily	Leucocytes	Remarks
		Rate	P-R (secs.)	T-wave			QRS change					
				I	II	III						
1925												
Oct. 5		83	0.24	−	+	+			100.4			
Oct. 14		100	0.38+	−	+	+			99.0	2.4	16,000	Admitted Oct. 4
Oct. 16		75	0.29	−	+	+			99.0	2.4	14,200	In bed
Oct. 18								12	99.0	2.4		
Oct. 20		78	0.28	−	+	+		11	99.0	2.4	11,800	
Oct. 23		71	0.37	−	+	+		8	99.0	3.6		
Oct. 27		75	0.25	−	+	+		10	99.0	3.6	11,800	
Nov. 7								9	99.8	3.6	11,500	
Nov. 10		68	0.37	−	+	+		4	99.1	4.8	10,700	
Nov. 17		68	0.37	−	+	+		8	99.6	3.6		
Nov. 24		68	0.38	−	+	+		10	99.8	0.0		
Nov. 30	I							8	99.6	3.6		
Dec. 5								14	98.8	3.6		
Dec. 7	II							12	98.8	3.6		
Dec. 8								1	98.8	3.6	10,000	In chair
Dec. 14		88	0.38	−	+	+		0	99.2	0.0	7,500	
Dec. 15	III							0	98.6	0.0		
Dec. 20								0	102.2	0.0	15,500	Splenic infarct
Dec. 23	IV	78	0.20	−	+	+	+	2	100.6	0.0		
Dec. 28								2	99.6	1.2	10,000	
Dec. 31		102	0.19	−	+	+		0	99.0	2.4		

TABLE II—CONT'D

DATE	RADIO-THERAPY	EKG. DATA						ATTACKS OF PAIN IN 24 HR.	HIGHEST TEMP.	SALICYLATE (GM.) DAILY	LEUCOCYTES	REMARKS
		RATE	P-R (SECS.)	T-WAVE			QRS CHANGE					
				I	II	III						
1926												
Jan. 4								1	99.0	1.2	7,000	
Jan. 12		71	0.24	−	+	+		2	99.0	2.4	11,000	
Jan. 19	V							1	99.0	2.4	7,500	
Jan. 21		50	0.24	−	+	+	+	1	98.8	2.4		
Jan. 26		68	0.25	−	−	+	++	1	99.4	2.4	8,000	
Jan. 27	VI	78	0.36	−	−	+	+	2	98.8	2.4		
Jan. 28		70	0.30	−	−	+	+	2	98.4	0.0		
Jan. 29		83	0.18	−	+	+	++	0	98.8	0.0		
Jan. 30		94	0.19	−	+	+		1	99.0	0.0		
Feb. 1		100	0.18	−	+	+	+	1	100.6	0.0		Splenic infaret
Feb. 2	VII	85	0.20	−	+	+		1	101.6	0.0		
Feb. 3		93	0.18	−	+	+		0	100.8	0.0		
Feb. 4		85	0.17	−	±	+	+	0	101.0	0.0		
Feb. 5		83	0.19	−	+	+	+	1	100.6	0.0	11,000	
Feb. 6		78	0.20	−	+	+		1	99.8	0.0		
Feb. 8		78	0.20	±	+	+		0	99.6	0.0	13,000	
Feb. 9	VIII							0	99.4	0.0		
Feb. 10		88	0.18	−	±	+	++	0	99.2	0.0		
Feb. 12		88	0.20	−	+	+	++	1	99.4	0.0		
Feb. 13		88	0.20	−	+	+		1	99.2	0.0		
Feb. 16		79	0.20	−	±	+	++	0	99.0	0.0		
Feb. 17		78	0.20	−	+	+	+	1	98.6	0.0		
Feb. 19								1	99.2	0.0	7,000	
Feb. 23		83	0.20	−	+	+		1	99.6	0.0		

I
II
III
1925
May 25
May 27 Radiotherapy I
May 28
June 8
June 10 Radiotherapy II
June 12

Fig. 1.

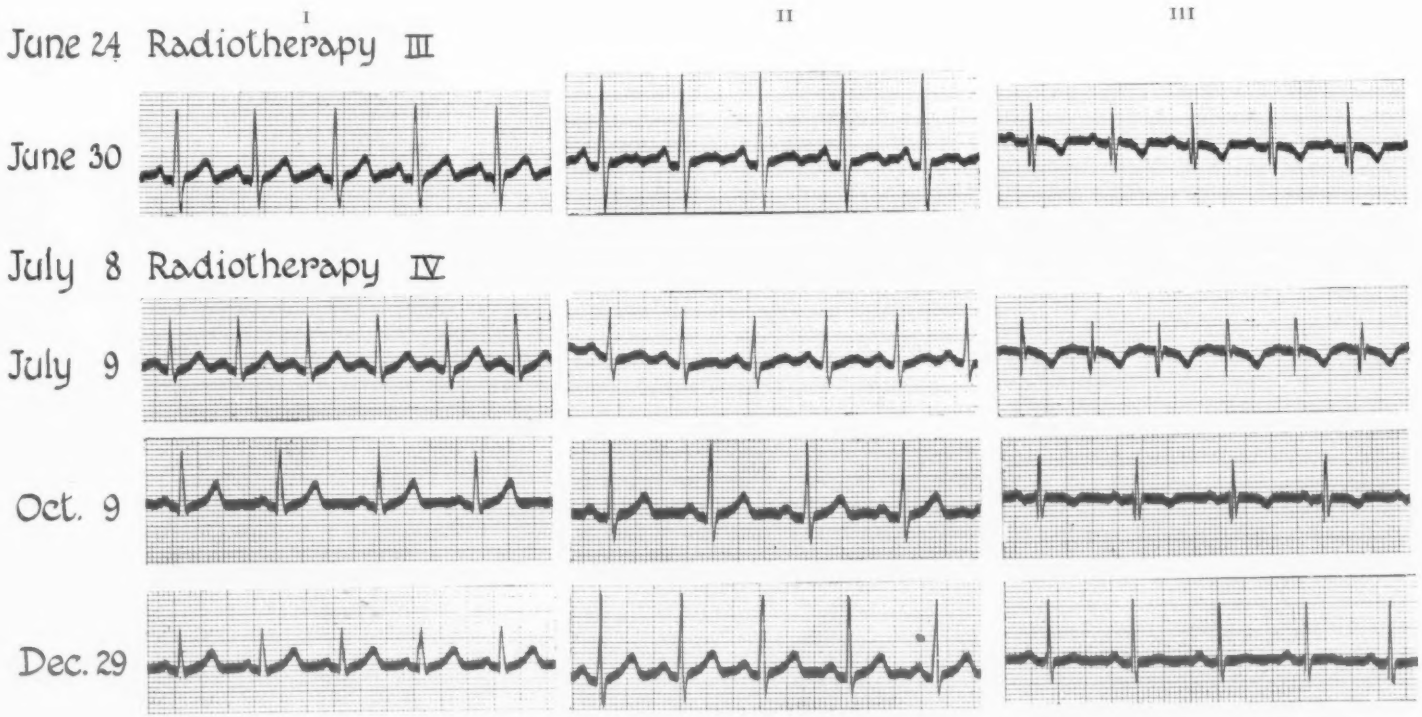

Fig. 1. (Continued.)

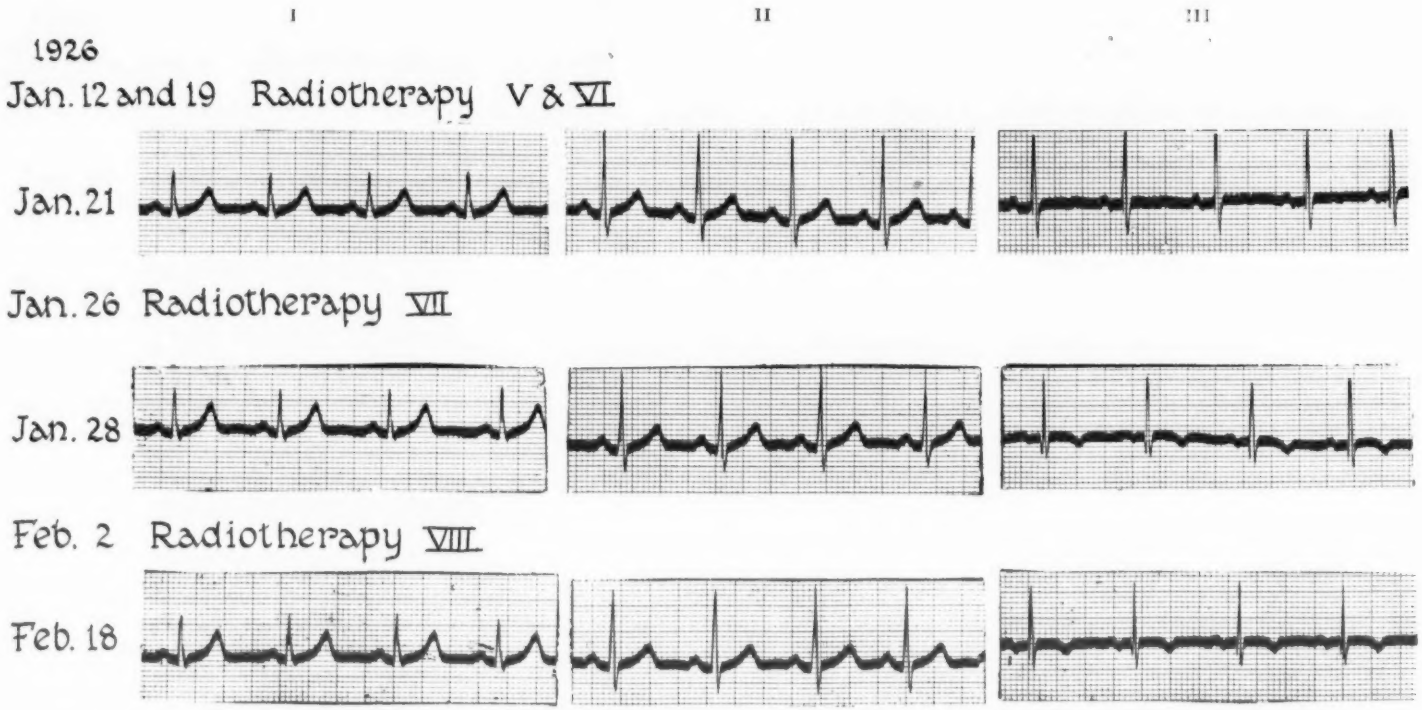

Fig. 1.—Effect of irradiation on the T-wave of the electrocardiogram. The record of May 25 serves as control. Following irradiation, the T-wave in Lead II becomes progressively flatter, in Lead III it becomes sharply inverted. The effect is most marked in the record of July 9. From July 22 to December 29, no roentgenotherapy was given. The record taken on the latter date shows a return of the T-waves to the forms observed in the control. Following a second course of irradiation, begun on January 12, the T-wave in Leads II and III undergoes changes similar to those seen after the first course, though of less marked degree. The same cycle of events was repeated a third time.

In the record of June 12 is seen a ventricular premature beat, occurring two days after the second roentgenotherapy.

The time of appearance and duration of the form changes in relation to irradiation were variable. As stated, T-wave inversion usually began soon after beginning treatment, progressed gradually, and lasted often for weeks or months. Alterations in QRS were sometimes temporary, but were occasionally permanent, as shown in Fig. 3. The

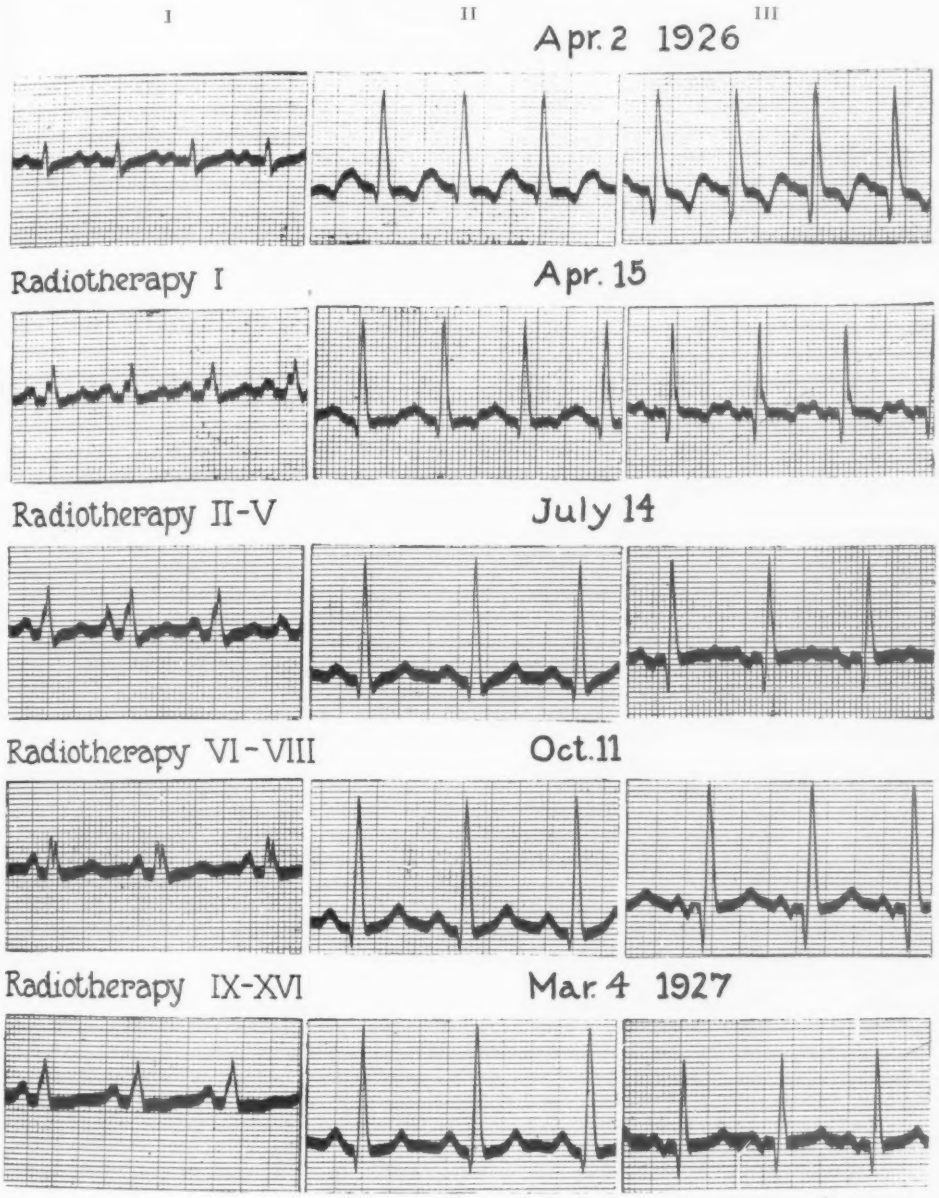

Fig. 2.—Effect of irradiation on the QRS group of the electrocardiogram. The changes are most marked in Lead I. The R-wave becomes sharply notched following irradiation and the notch changes its form and position in successive graphs.

The record also shows alterations in the P- and T-waves in Leads II and III. After showing changes continuously over a period of sixteen months, the form of the curves became constant and has remained so for eight months.

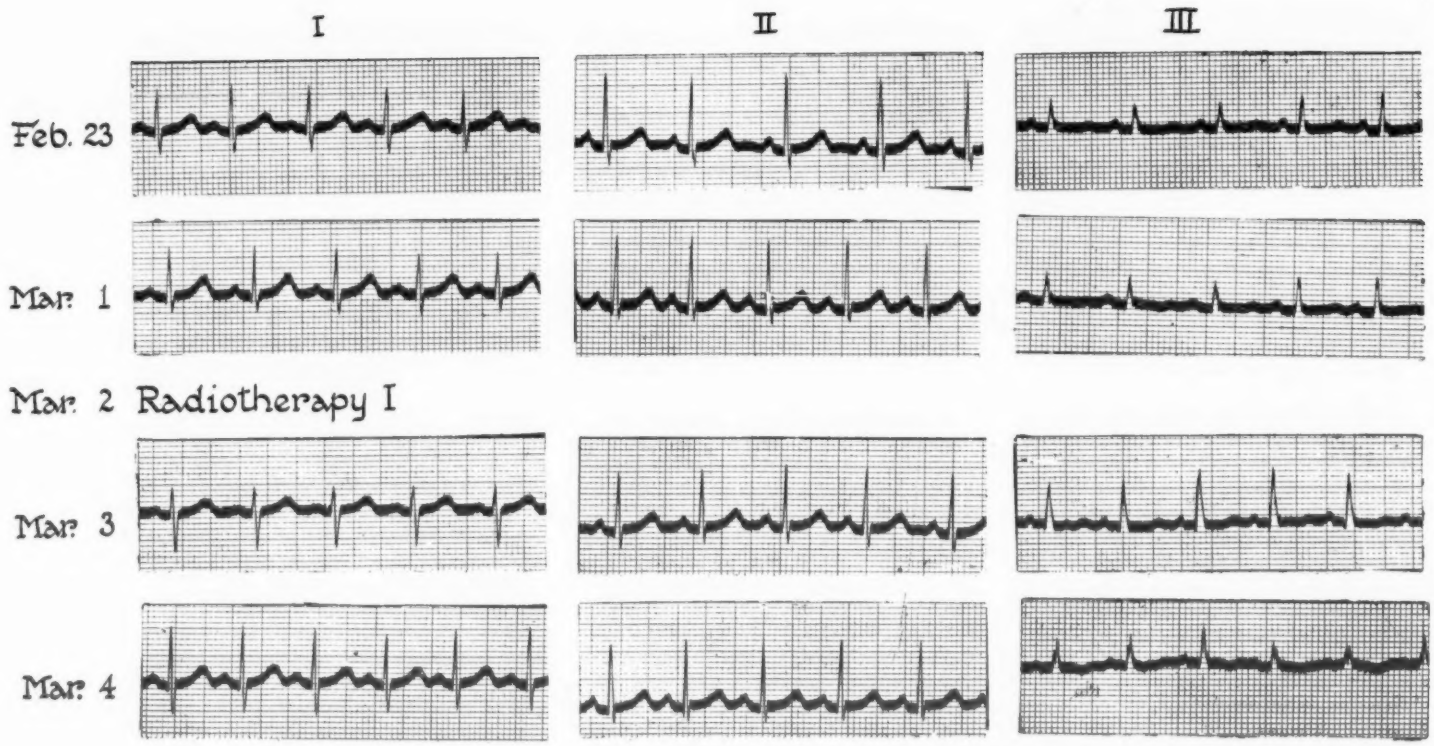

Fig. 3.—Effect of irradiation on the electrical axis. Two control records are shown, taken one week apart. Following irradiation, there is a shift of the electrical axis to the right, resulting in the sequence known as right ventricular preponderance. The change is transitory, and two days after irradiation, the graphs resemble those seen in the controls.

other changes appeared soon after an exposure and were evanescent, disappearing often in the course of a few days.

Effect on Clinical Conditions.—Because cases of varying degrees of severity were included in the group, representing different stages of rheumatic infection, it was to be expected that the results would be variable. It is also possible that some of the patients did not receive a sufficient number of treatments. Of the thirty patients, twenty-one (70 per cent) were considered improved at the end of the follow-up period. Variability and uncertainty in the clinical course of rheumatic fever are well known. To propose to establish the value of a therapeutic procedure on the basis of a small series of cases, however carefully observed, is clearly unsound. It is our impression that in many of these cases, improvement was definitely related to roentgenotherapy. The change in condition was evidenced by cessation of fever, fall in heart rate, disappearance of leucocytosis, and gain in weight. In most of the cases, salicylates and drugs of the cinchophen group were given. Where possible, a control period, free from all other therapy, was carried out prior to starting irradiation. The five patients who died had advanced lesions and continuously active rheumatism with progressive myocardial failure. Some of the instances of improvement were striking. Seven patients had paroxysms of severe cardiac pain. Five of these were relieved during the follow-up period. The results can best be indicated by citing briefly a few illustrative cases, including both favorable and unsuccessful examples.

Case 1.—A girl of thirteen years gave a history of recurring arthritis for four years, with dyspnea and edema for nine months. The heart was large and showed a double mitral lesion. She had been in the hospital for nine months, during which there was continued fever, tachycardia, chest pain, and leucocytosis, although the joint manifestations were negligible. Salicylate and neocinchophen were administered repeatedly in large doses, and several small transfusions were given. Heart failure was controlled with digitalis. All discoverable foci of infection were carefully eradicated. Low grade infection persisted and appeared to be chiefly in the heart. Five days after the first irradiation, the temperature fell to normal, with parallel decrease in heart rate. With but few minor setbacks improvement continued. During the next eleven months she received thirteen roentgen treatments. Following roentgenotherapy, the electrocardiograms showed a striking shift in electrical axis on two occasions, and slight changes in P, T, and the R-T interval at other times. Auricular premature beats were noted once. It is now over three years since radiotherapy was begun, and she has had none for over two years. The electrocardiogram has been constant in form for eighteen months. There has been no recrudescence, she has grown and gained weight, and goes to public school. The relationship between irradiation and the onset of improvement seemed definite; and the course since leaving the hospital has been much more favorable than might have been anticipated in this type of case.

Case 2.—A boy of sixteen years, with enormous heart, double mitral lesion, and aortic insufficiency, had had recurring rheumatic infection since the age of twelve. Heart symptoms appeared at the age of thirteen. Tonsillectomy was performed

at the age of ten. For three years he had been bedridden, suffering from severe paroxysms of heart pain. During these attacks his blood pressure would often rise to above 200 mm. Hg. and he would break out in a cold perspiration. Nitroglycerin afforded relief. At the time of admission to the hospital, he was having as many as twelve of these paroxysms in the course of twenty-four hours and was taking up to 20 tablets of nitroglycerin daily. There was slight fever. The leucocytes were 16,000. The electrocardiogram showed sinus rhythm, marked left ventricular preponderance, prolonged P-R interval, inversion of T_1 and notching of R_2. Clearly, there was marked myocardial damage with active lesions present in the heart muscle. His course and response to irradiation are shown in Table II. Of greatest interest is the relief from paroxysms of pain. Conduction time (P-R interval) returned to within normal limits. Fever and leucocytosis likewise subsided except when embolic infarction of the spleen occurred on two occasions. The electrocardiogram, constant in form prior to beginning roentgenotherapy, began to show changes after the third treatment, shortly after the onset of clinical improvement. Salicylate was given only in small doses because it was poorly tolerated; it seems improbable that it played a rôle in the relief of pain.

Unhappily, the attacks of pain recurred after four months of relative comfort. Left cervical sympathectomy was then done under local anesthesia. The boy died three days later of myocardial failure. Necropsy was not permitted.

CASE 3.—A girl of eighteen years (a private patient of Dr. D. W. Atchley), had rheumatic fever annually from the ages of seven to fourteen, and again at seventeen. She was admitted to the hospital complaining of slight arthritis, dyspnea, and paroxysms of severe heart pain, with radiation to the left arm. Dyspnea had been present for one year, the pain for one month. The heart was greatly enlarged. There were signs of mitral stenosis and insufficiency but no aortic valve lesion was made out. During a period of seventeen months twenty-five irradiations to the heart were given. The form of the electrocardiogram changed frequently during the first sixteen months, then became constant and has remained so for eight months. The attacks of precordial pain have entirely disappeared, the functional capacity of the heart has improved, and the patient is working in a secretarial position. In this case, complete relief from pain was afforded and a smouldering carditis was apparently converted into an inactive myocardial fibrosis.

CASE 4.—A colored girl of eleven years had her first attack of chorea and arthritis two years before entering the hospital. Tonsillectomy was performed shortly after admission. Fever was continuous, though not high; the heart was large, with double mitral lesion. Numerous subcutaneous nodules were present. Five irradiations were given during a period of three months. There was slight flattening of the T-waves in Leads II and III, and transitory right preponderance appeared after the third treatment. Although constantly in bed, heart failure and signs of a tricuspid lesion developed. New crops of nodules appeared from time to time and leucocytosis was persistent. She died ten months after the first roentgenotherapy, with all the evidences of progressive, active rheumatism and with myocardial failure. Necropsy was not performed. In this case, a severe rheumatic infection was entirely uninfluenced by roentgen irradiation of the heart.

In view of these experiences, what conclusions may be drawn as to the type of patient most suitable for roentgenotherapy? Early cases, in the first attack, with beginning cardiac involvement obviously offer the best material. More advanced cases, with paroxysmal heart pain, have been afforded relief in five of seven cases. In a number of cases

of low-grade infection with predominantly cardiac involvement, it appeared that the infection subsided. Patients with advanced mechanical defects and outspoken cardiac failure, as well as those with signs of overwhelming rheumatic infection, have proved unsuitable subjects.

Effect of Roentgen-ray Therapy on Heart Size.—No changes were observed in the teleroentgenograms which could be related to irradiation. Particular mention is made of this point because Beeck and Hirsch[2] described diminution in the width of the aorta in one of their cases, after irradiation.

TABLE III

UNPLEASANT EFFECTS IN 30 PATIENTS RECEIVING IRRADIATION OVER THE CARDIAC AREA

Nausea and vomiting	8 cases
Increased chest pain	3 cases
Headache	2 cases
Exacerbation of fever	1 case

Unpleasant Effects.—In no instance was there evidence that the heart was injured or the course of the disease unfavorably influenced. Fourteen patients had mildly unpleasant effects which are shown in Table III. Nausea, vomiting, and headache are familiar radiation reactions. Increased chest pain and fever may, perhaps, be attributed to a disturbance induced in specific rheumatic lesions.

EFFECT OF IRRADIATION OF THE HEART IN SUBACUTE BACTERIAL ENDOCARDITIS

A limited number of irradiations were given to four patients with nonhemolytic streptococcus endocarditis. Three of the patients received three treatments, the fourth patient only two. There was no demonstrable effect either on the electrocardiograms or on the fatal progress of the disease. All of the patients died within three months. One patient, who received two irradiations, came to necropsy. No changes were found in the heart which could be ascribed to irradiation.

POSSIBLE MODE OF ACTION OF IRRADIATION ON THE RHEUMATIC HEART

As the result of therapeutic experience with various forms of local infection, as stated in an earlier paragraph, it appears that roentgen irradiation modifies the tissue response to the infection in a manner favorable to recovery. In this connection the experiments of Bass[12] are suggestive. He injected rabbits intravenously with a culture of virulent streptococci. Animals irradiated over the abdomen with 50 per cent of the skin erythema dose of x-rays lived from five to ten days, whereas nonirradiated animals died in from one to three days. The action of the rays, in Bass' opinion, is general as well as local, and is probably brought about through activation of the reticulo-endothelium by cellular decomposition products.

Renewed interest in the rôle of allergy in rheumatic fever has been stimulated by the recent work of Swift and his collaborators.[13] They have formulated the hypothesis that in this disease the tissues of the body have become allergic to the products of certain nonhemolytic streptococci, the allergizing substance being produced in a focus such as the tonsils. Sensitization is not necessarily specific for any particular variety of streptococcus.

It has been shown that radiant energy (ultraviolet light) modifies the reaction of the skin to certain bacterial products when these are injected into it. Thus, the intradermal tuberculin test in guinea pigs and patients gives a lessened reaction when the injected area is treated locally with short exposures of ultraviolet rays, either before or after injection.[14] Such a phenomenon may be interpreted as indicating a process of desensitization. Is it not conceivable that in rheumatic fever roentgen irradiation serves to desensitize the tissues of the heart to an allergizing substance, thereby favoring the subsidence of existing lesions and, for a time at least, preventing further cardiac damage? The action of the rays may be local, or general, or perhaps both.*

CONCLUSION

Cardiac involvement constitutes the chief menace in rheumatic fever. As yet, neither the causative agent of the disease nor a specific remedy for it are at hand. In certain cases of rheumatic carditis, roentgen irradiation of the heart appears to exert a favorable influence. It is possible that in patients having their first attack of rheumatism, with or without evidence of cardiac involvement, irradiation may be useful in minimizing the danger of damage to the heart.

SUMMARY

1. Thirty patients with rheumatic heart disease were given 249 roentgen irradiations over the cardiac area. The machine setting was calculated to yield about 10 per cent of the erythema dose distributed throughout the heart muscle. In addition to noting changes in clinical condition, frequent electrocardiograms and numerous teleroentgenograms were made.

2. Following irradiation, changes in the form of the electrocardiogram were observed in 17 of the 30 cases. It is believed that these changes were due to the effect of irradiation on the myocardium, with modification of the rheumatic lesions.

3. Of the 30 cases, 21 (70 per cent) showed clinical improvement at the end of the follow-up period. Three improved temporarily, 1 was

*Since this article was prepared for publication, Zinsser and Yu (*Arch. Int. Med.*, 1928, xlii, 301) have adduced evidence which lends support to the view that focal infection, with consequent sensitization of the body, is the cause of many of the manifestations of rheumatic fever. They have isolated streptococci from the myocardium in one case and from the spleen in two cases at necropsy, and suggest that these foci may represent the localization of the bacteria during periods of quiescence.

unimproved, and 5 died. Those cases terminating fatally were all instances of continuously active rheumatism, with advanced lesions and progressive cardiac failure.

4. In 5 of 7 patients with paroxysms of severe heart pain, relief from this symptom followed roentgenotherapy.

5. Early cases, in the first attack of rheumatic fever, offer the best chance for success in therapy. In a number of cases with low-grade infection, predominantly cardiac, it appeared that the infection subsided following roentgenotherapy. It seems likely that at least one series of four treatments is necessary to initiate improvement. More prolonged therapy is probably desirable.

6. No changes were observed in the teleroentgenograms which could be ascribed to the effects of irradiation.

7. Unpleasant symptoms were noted in 14 cases. These were due, for the most part, to radiation reactions. In no instance was there evidence of injury to the heart or an unfavorable effect on the course of the disease.

8. In 4 cases of subacute bacterial endocarditis due to nonhemolytic streptococcus, roentgen irradiation of the heart caused no change in the form of the electrocardiogram, nor did it arrest the fatal progress of the disease.

9. It is suggested that in rheumatic fever, roentgen irradiation of the heart may serve to desensitize the tissues of the heart to an allergizing substance, thereby favoring the subsidence of existing lesions and preventing further cardiac damage.

10. In patients having their first attack of rheumatism, irradiation may be useful in minimizing the danger of damage to the heart.

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OBSERVATIONS ON CERTAIN ETIOLOGICAL FACTORS IN RHEUMATISM*

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THE importance of acute rheumatic fever and its accompanying condition, rheumatic heart disease, is being increasingly recognized as a public health problem. Efforts are constantly in progress to form a true picture of the disease from the standpoints of epidemiology, infectivity, communicability, and bacteriology. This study is offered, not for any definite conclusions which can be drawn, but to present certain facts which may be added to other facts, and in the final analysis give us accurate knowledge of rheumatism and its natural history.

The term "rheumatism" used in this paper refers to chorea and acute rheumatic fever. The material was drawn from the Children's Medical Service of Bellevue Hospital in New York City, both ward cases and cases from the Huddleston Memorial Cardiac Class. The cases from the wards include all admissions for rheumatism in the years 1923 to 1927, and were not selected in any sense. The records of about 2000 cases which had gone through the cardiac class were reviewed, and accurate data found on about 500 of these. The patients were children up to the age of thirteen years. The points considered were: (1) race, (2) sex, (3) age at onset of rheumatism, and (4) seasonal incidence.

TABLE I

RACE	PER CENT IN CARDIAC CLASS	PER CENT IN GENERAL PEDIATRIC CLINIC
Italian	23.5	19.56
Jewish	21.94	27.4
American	19.00	14.48
Irish	15.8	4.3
German	5.33	4.1
Polish	3.95	3.7
Hungarian	2.76	1.17
Austrian	1.58	4.7
English	1.38	0
Spanish	1.18	5.09
Greek	0.98	3.3
Czecho-Slav	0.98	1.6
Colored	0.59	1.6
Finn	0.19	0
Ukranian	0.19	0
Armenian	0	5.47
Roumanian	0	2.34

*From the College of Physicians and Surgeons, Columbia University, and the Childrens' Medical Service, Bellevue Hospital and the Huddleston Memorial Cardiac Class.

RACE

It is well known that rheumatism and rheumatic heart disease are common in certain countries; namely, Great Britain, North America, and Germany, while certain races, such as the Chinese, Japanese and natives of India are seldom affected. This suggests the possibility that climate may be a factor in the incidence of these conditions, but this is difficult to determine conclusively. Racial susceptibility must be considered as a possible factor, but here also it is difficult to draw fixed conclusions in the absence of a very large number of cases. If we can show that a certain racial stock in this country has a high incidence, while in its own country it has a low incidence, it is reasonable to believe that climate is more of a factor than race.

Table I shows an analysis by race of 506 children in the cardiac clinic at Bellevue compared with the race of 511 children in the general pediatric clinic. This demonstrates that although the Italians form only 19.56 per cent of the population of the general clinic, they comprise 23.5 per cent of the cardiac class. Similarly, 27.4 per cent of the children in the general clinic are Jewish, while only 21.94 per cent of the cardiacs are of this race. This suggests that the Italians in New York City are somewhat more susceptible to rheumatic heart disease than are the Jews of this city. A more striking comparison is shown in the figures for the Irish. Of the cardiac patients, 15.8 per cent are Irish, although only 4.13 per cent of the patients in the general clinic are of this race. The Irish in Ireland do not have a high rate for heart disease. Again, while there were no English among the sample from the general clinic, 1.38 per cent of the cardiac patients were English. Native born Americans form 14 per cent of the general clinic and 19 per cent of the cardiac clinic. The type of population of the neighborhood in which a clinic is located may affect the races which attend the clinic, but Bellevue, which is a municipal hospital, draws its patients from all parts of the city as well as nearby suburbs, so that this factor does not operate as it would in a strictly neighborhood clinic.

These findings suggest that in New York City certain races are more susceptible to rheumatism and rheumatic heart disease than certain other races, and that climate may be a factor.

SEX

Females are slightly more frequently affected with rheumatic heart disease and rheumatism than males. Of the 506 cardiac children from the out-patient department, 214 were boys and 292 were girls. The combined percentages for Bellevue and one other smaller clinic were, boys 44 per cent, girls 56 per cent.

AGE AT ONSET

The figures for this part of the study apply only to cases where a definite date could be obtained for the first attack of chorea or acute rheumatic fever. No attempt was made to include cases where the first rheumatic manifestation was an endocarditis.

Fig. 1 shows the curve for 623 cases of both sexes. The peak of this curve occurs at nine years. When the sexes are separated, a rather interesting fact is disclosed; namely, that the peak for the boys comes two years earlier (i.e., at seven years) than the peak for

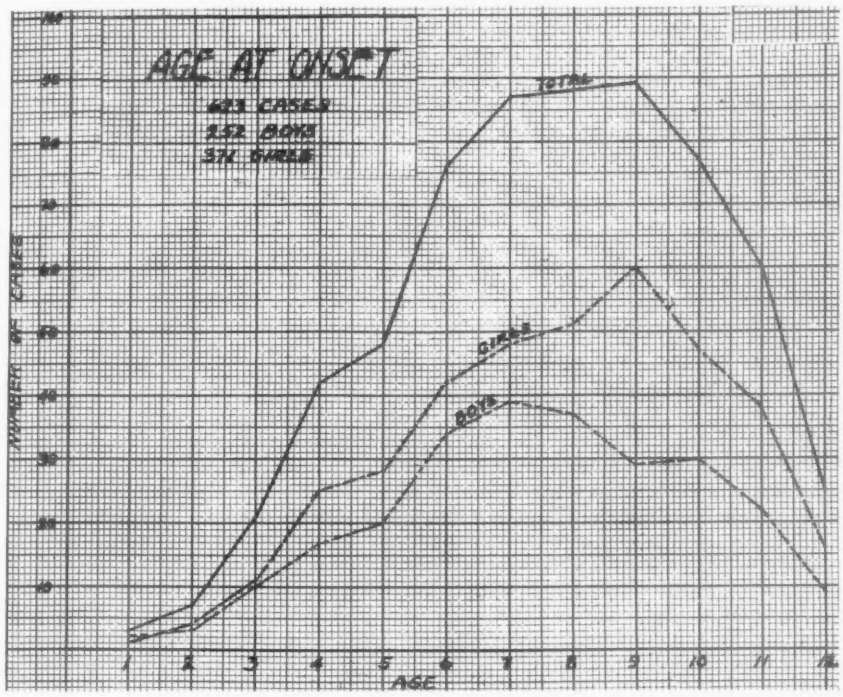

Fig. 1.—Combined ward and out-patient department cases.

the girls (nine years). It was also found that among 253 girls with rheumatic heart disease 21 per cent gave no history of chorea, acute rheumatic fever, or growing pains prior to the discovery of heart disease, and that of 174 boys, 14 per cent gave no such history. Since we know that a greater number of girls than boys develops rheumatic heart disease, this suggests that girls have an inherently greater susceptibility, so that an infection which is not sufficiently overwhelming to produce an attack of acute rheumatic fever may give an endocarditis without marked symptoms. To state it in another way, rheumatism more frequently manifests itself in girls primarily as an endocarditis than it does in boys.

SEASONAL INCIDENCE

As had been expected, a definite seasonal incidence for rheumatism was found. The greatest number of attacks begins in April, the next greatest in May. This does not coincide with the findings in Great Britain.[1] Fig. 2 gives the curve for 584 cases of chorea and acute rheumatic fever according to the month in which the attacks began. The data were taken from the hospital cases from 1923 to 1927 (389 cases) plus the out-patient department cases, which were not selected by years. Since the curves made for these two samples separately were seen to be similar, the figures were combined to make a single

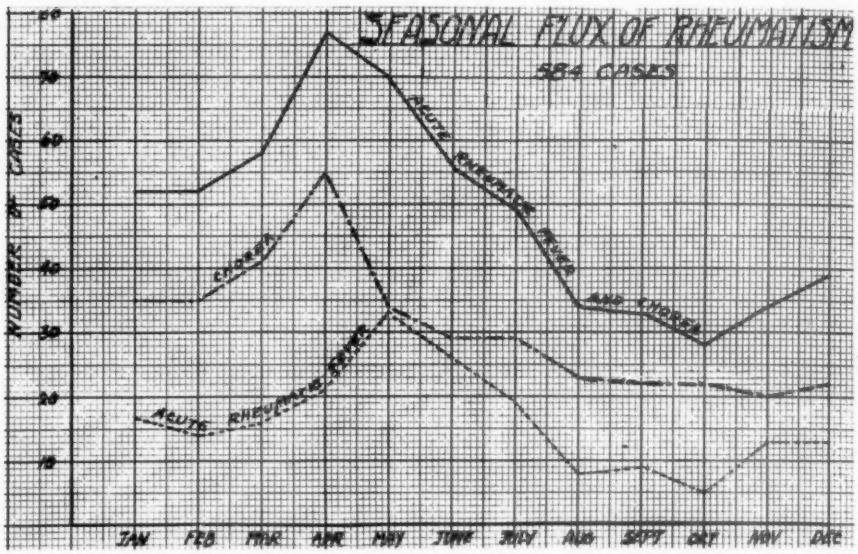

Fig. 2.—Combined ward and out-patient department cases.

curve. In this same figure the curves for chorea and acute rheumatic fever are separated. There is a lag of acute rheumatic fever compared with the curve for chorea, i.e., the peak of the curve for chorea occurs in April, and the peak for acute rheumatic fever in May.

In Fig. 3 are compared the findings from 459 cases taken from two hospitals in London and one in Glasgow,[1] and the 584 cases from Bellevue Hospital. The British figures show that 12 per cent of their cases occurred in November and 11 per cent in January, while June and July had the lowest percentage, namely, 5 per cent. In contrast to this the New York figures show that 13 per cent of the cases occurred in April, and 12 per cent in May, with October as the low month with 5 per cent.

METEOROLOGICAL CONDITIONS

It was thought that the difference in seasonal incidence of rheumatism found in London and Glasgow, and in New York, might be explained by meteorological conditions. For this reason data on the temperature and precipitation in New York City were obtained from the Weather Bureau, with the expectation of finding high precipitation in the months of the year when the cases were most numerous.

The general impression seems to be that most cases of rheumatism occur during damp cold weather, and this belief appears to be largely

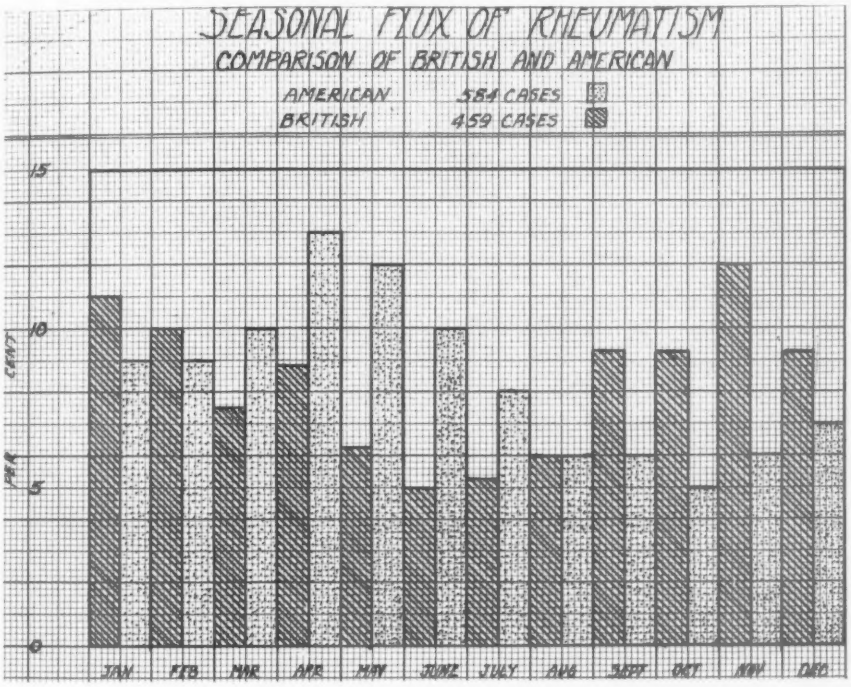

Fig. 3.—Taken from "Social Conditions and Acute Rheumatism" with American findings inserted for comparison.

based on the work of Young[2, 3] in England. He studied the annual rainfall and temperature in 55 counties in England and Wales in relation to the standardized death rate from rheumatic fever among individuals fifteen years of age and up. He states that "there is a distinct tendency for excess in rainfall to be associated with an increased death-rate from, and presumably an increased prevalence of, rheumatic fever. . . . the death-rate is higher and presumably the malady is more prevalent with an excess of cold weather during the year." Varying opinions had been stated before Young's study was made. Newsholme (quoted by Young) had come to the conclusion that heavy annual rainfall is associated with a low amount of rheu-

matic fever and small rainfall with an excessive amount, though he found no exact proportion. He also found that, on the whole, high temperature favored an increased amount of rheumatism. Gabbett (quoted by Young) concluded that it was difficult to make any connection between the state of the weather and the prevalence of disease in individual years but that the cases were numerous at the time of year when there was heavy rainfall and low temperature, i.e., at the end of autumn. Greenwood and Thompson (quoted by Young) concluded that rheumatism is associated with dry weather.

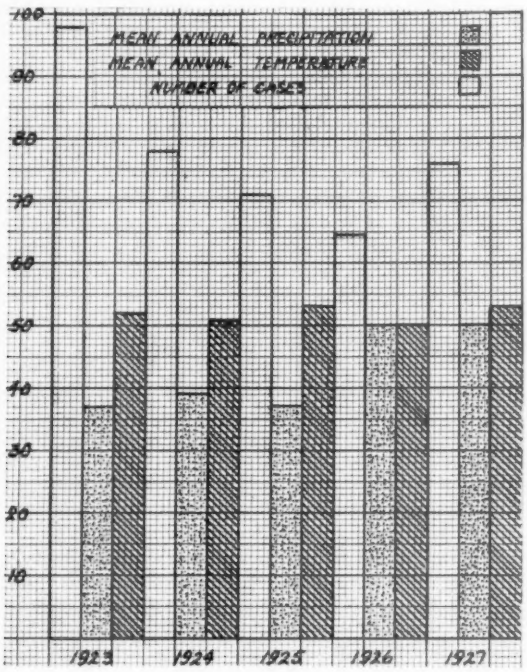

Fig. 4.—Comparison of mean annual temperature and precipitation 1923 to 1927 and number of cases admitted to wards during these years.

The figures used in this study are for precipitation, which includes both rain- and snow-fall.

Fig. 4 compares the mean annual temperature and the mean annual precipitation for the years 1923 to 1927, with the number of ward cases on the children's service at Bellevue Hospital for these years. The year which held the greatest number of cases had the lowest precipitation; the year with the fewest cases had the highest precipitation. There is little variation in the mean temperature, but the year with the highest mean temperature brought next to the lowest number of cases to the hospital.

Fig. 5 gives the monthly curve for the children admitted to Bellevue during the years 1923 to 1927, compared to the monthly mean precipi-

tation and temperature averaged for these years. Before combining the five years and getting the average, curves were made for each individual year, with results not essentially different from the averaged results. These curves appear to show that the greatest number of cases occur in the months when the precipitation is lowest and the temperature rising. This is exactly the opposite of what had been anticipated.

No conclusion can properly be drawn from this or any similar study as to the effect of meteorological conditions on the incidence of rheumatism. When accurate morbidity statistics are obtainable, it is pos-

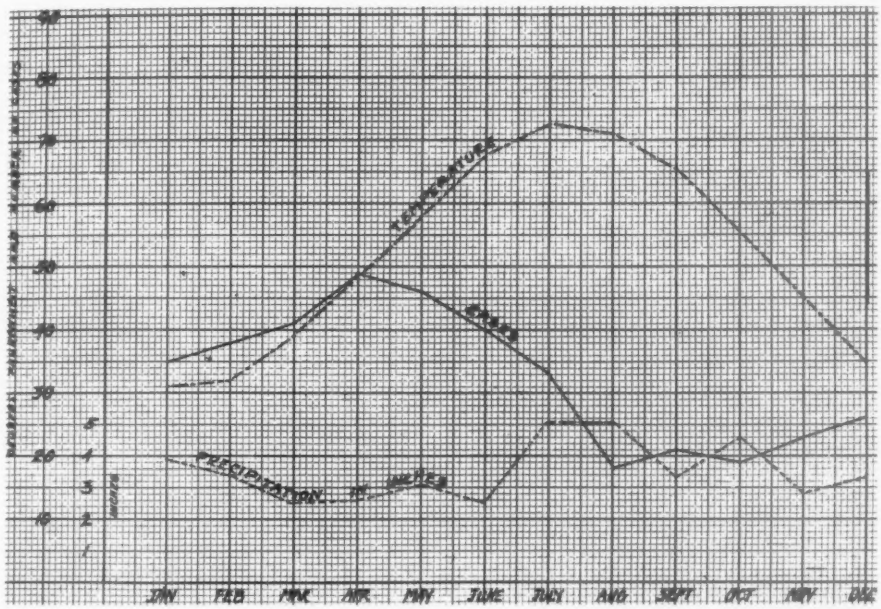

Fig. 5.—Monthly mean temperature and precipitation averaged for years 1923 to 1927, and number of cases admitted to wards during the months of these years.

sible that some correlation will appear, but for the present it can only be said that there appears to be little if any relation between the seasonal incidence of rheumatism, and precipitation, and temperature.

SUMMARY

Analysis by race of 506 children in the cardiac clinic at Bellevue Hospital and 511 children in the general pediatric clinic indicates that certain races in New York City, namely, Italian, Irish and native-born Americans, are somewhat more susceptible to rheumatism than certain other races. Certain other races, namely, Spanish, Armenian, and Jews, seem to be less susceptible.

Females are slightly more frequently affected with rheumatic heart disease than males.

The age at which most cases of rheumatism begin, without considering sex, is nine years. The average age at onset for boys is seven years, for girls nine years.

Twenty-one per cent of girls with rheumatic heart disease gave no history of rheumatic infection before the discovery of heart disease, while only 14 per cent of the boys gave no such history.

There is a definite seasonal incidence of rheumatism in New York City, which shows little variation in individual years. In general, the spring months show the highest incidence. For the five-year period studied, April and May contained the greatest number of cases. No correlation could be made between meteorological conditions and monthly incidence of rheumatism. In general, the height of the rheumatic season occurred at the time of year when the precipitation was lowest and the temperature rising, a finding contrary to that to be expected if Young's conclusions have general applicability.

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THE CLINICAL SIGNIFICANCE OF ABERRANT VENTRICULAR RESPONSE TO AURICULAR PREMATURE BEATS AND TO PAROXYSMAL AURICULAR TACHYCARDIA*

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INTRODUCTION

ONE of the most serious electrocardiographic findings in the study of heart disease is that of intraventricular block, either slight in degree or full bundle-branch block, a finding which represents important damage in the coronary circulation or in the myocardium. The fact that in experimental studies, aberrant ventricular responses (that is, intraventricular block) to auricular premature beats are obtained more readily when slight conduction changes are present due to asphyxia,[1, 4] and our own observation of this phenomenon in some patients with serious heart disease, suggested the possbility that aberrant ventricular responses to auricular premature beats may represent serious trouble with the conducting system or with the muscle of the heart. To throw further light on this point, the electrocardiograms of three hundred and eighty-seven consecutive cases showing auricular premature beats were carefullly reviewed. The patients concerned were in the wards or out-patient department of the Massachusetts General Hospital or were referred as private patients for special study. The electrocardiograms were taken over a period of thirteen and one-half years (1914 to 1928). One hundred and seven of these three hundred and eighty-seven cases showed aberrant ventricular responses of varying degrees. The electrocardiograms and the cases from which these records were obtained have been analyzed and the cases followed so far as possible.

In a clinical study of the ventricular response to auricular premature beats in a few cases from this laboratory some years ago White and Stevens[2] concluded that the degree of aberration in the ventricular response depends largely upon the degree of prematurity. Lewis[3] in 1909-10 first observed aberrant ventricular responses to auricular premature beats, without attempting to give an explanation. This same author[4] again in 1911-12 reported additional cases and first suggested the name "aberrant ventricular response," proposing the explanation that the appearance was caused by block in the ventricular portion of the conducting system. His first case by

*From the Cardiographic Laboratory and Cardiac Clinic of the Massachusetts General Hospital.

this time had been observed for two years. The degree of prematurity was considered important in relation to the degree of aberration. This is commented upon by Rosenthal[5] who reported a case at the same time. In 1924 in a paper on incomplete bundle-branch block, Stenström[6] reviewed the literature on aberrant ventricular response to auricular premature beats and concluded from experimental studies and clinical observations that this phenomenon may be aptly compared to the different stages in partial A-V block. He did not study the clinical significance of this finding. Lewis[7] has fully summarized experimental and clinical observations on this point up to 1925. The recent literature on premature beats has been chiefly concerned with the theories about their origin or with treatment. E. C. White[8] has studied one hundred cases of all varieties of premature beats, 45 per cent being associated with definite heart disease, and 55 per cent with no heart disease. D'Irsay[9] reviewed one hundred cases seen in hospital practice and made especial distinction between unifocal and multifocal origin of extrasystoles, presuming the former to be neurogenic and the latter due to an organic myocardial degeneration. The "multifocal" extrasystoles in that author's series showed a higher mortality and were associated with "some myocardial lesion, detected either by electrocardiograph or by autopsy." Wenkebach,[10] in his textbook, states that aberration of the ventricular complex following auricular premature beats is due to a variable recovery period and is without especial significance.

RESULTS OF PRESENT STUDY

Selecting from the total series of our three hundred and eighty-seven cases showing auricular premature beats those one hundred and seven cases with aberrant ventricular responses, we have divided them into four classes according to the degree of aberration shown. Several electrocardiograms showing auricular premature beats were sometimes obtained from a single case. Such a case has been grouped according to the greatest degree of abnormality of ventricular response shown to auricular premature beats. Altogether there were four hundred and forty electrocardiograms taken of the one hundred and seven cases showing abnormal ventricular responses to auricular premature beats. In Class I two cases showed normal as well as slightly aberrant T-waves following auricular premature beats, while Classes II, III and IV included twelve, sixteen and three cases respectively which showed at the same time lesser degrees of aberrant response than that for which they were placed in the given class. Class I (Fig. 1) includes only those cases (16) with but a slight change in the T-wave following an auricular premature beat, Class II (Fig. 2) those cases (55) showing slight changes either in the QRS complexes alone or in both QRS and T. Slight changes in the T-wave consist of

depression of the wave as compared to other T-waves following normal auricular waves in the same tracing. Slight QRS changes consist of heightening or shortening of R, or of deepening or shortening of S as compared with those QRS complexes which follow normally placed P-waves. Class III (Fig. 3) (30 cases) consists of moderate (more than slight) changes in QRS and T-waves following auricular premature beats. Finally, Class IV (Fig. 4) is made up of six cases exhibiting very marked changes in amplitude with widening of the QRS interval and usually with profound changes in the T-wave. Forty cases have

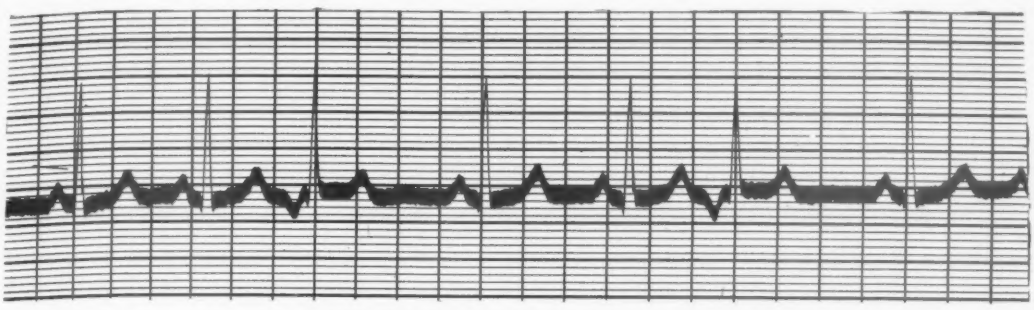

Fig. 1.—The third and sixth ventricular complexes illustrate the type of ventricular response to auricular premature beats included in Class I (referred to in the text); slight changes in T-wave and S-T interval only. Lead II. (In this as in the other illustrations time intervals equal fifths of a second. Amplitude is expressed by divisions marking off intervals of 10^{-4} volt.)

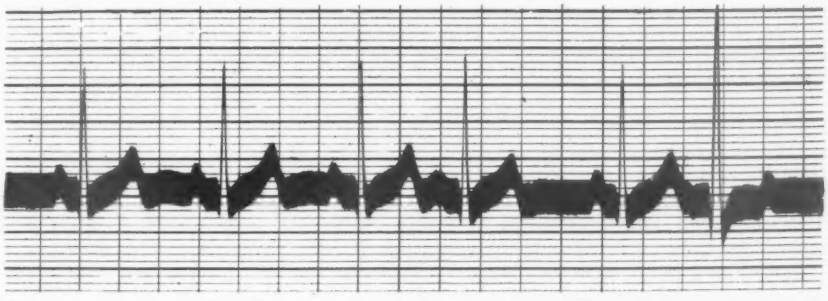

Fig. 2.—The fourth ventricular complex represents those premature beats used as controls while the sixth complex represents Class II, slight changes in both QRS and T-waves. Lead II.

been studied as "normal controls" (Fig. 2)—that is, normal so far as the ventricular response to auricular premature beats is concerned.

The age and sex distribution for this series is given in Table I. Both in the series of cases with varying degrees of aberrant responses and in the control group showing normal responses, the occurrence is greater among males (56 to 36 in the former, 27 to 11 in the latter). The age distribution for all four classes as well as for the normal controls is approximately the same, in all cases the incidence of the auricular premature beats being greatest between the ages of fifty and seventy years.

The relation of degree of prematurity to degree of aberration is demonstrated very clearly in Table II. The figures give the average of the percentage relation of time intervals of P-P′ to P-P; those premature beats represented by the smaller figures have fallen earlier in diastole.

It is interesting to note here the occurrence of intraventricular block during the course of *paroxysms of auricular tachycardia.*

Transient disturbances of this nature of less importance have been noted; as for example in the case of a nurse who developed for a few

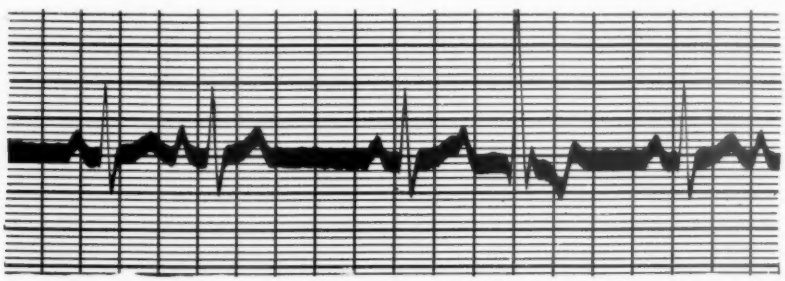

Fig. 3.—The fourth ventricular complex falls in Class III, moderate QRS and T-wave changes. The second ventricular complex shows essentially normal QRS and T-waves. Lead II.

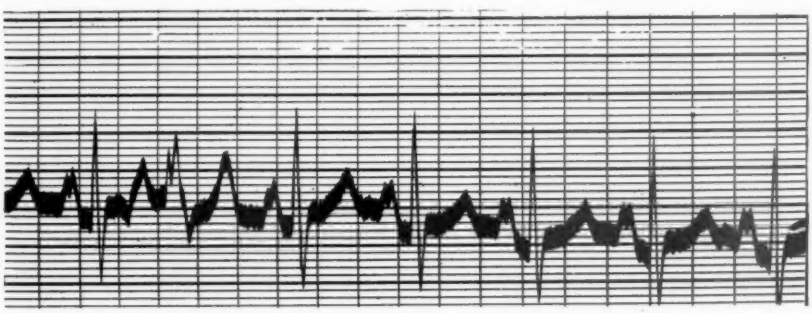

Fig. 4.—The second ventricular complex shows marked aberration, Class IV. Lead II.

minutes left bundle-branch block at the height of a paroxysm of auricular tachycardia of extreme degree (both auricular and ventricular rates were 273), reported by White and Stevens.[2] Now, thirteen years later, this nurse is working and in good health except for rare intervals of disturbed heart rhythm lasting a few hours at a time (ectopic auricular tachycardia, generally with auriculoventricular block). Three other cases, four in all, of aberration in the ventricular complexes in the course of a paroxysm of auricular tachycardia have been observed in a series of 73 cases of paroxysmal auricular tachycardia. One of these patients, a man aged sixty-four years (diagnosis rheumatic heart disease, irritable heart, aortic re-

gurgitation, Stokes-Adams syndrome, partial A-V block, S-A block, paroxysmal tachycardia, auricular and ventricular premature beats), has had heart trouble since rheumatic fever forty-three years ago. Stokes-Adams symptoms have been present about eight years. Our

TABLE I

SEX AND AGE DISTRIBUTION*

CLASS	M.	F.	AGE 1-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
I	7	5		1			3	2	5	1	1
II	26	18	1	6	4	1	8	8	8	6	
III	19	11		1	4	2	4	6	3	1	
IV	4	2			1			1	1		
Total	56	36	1	8	9	3	15	17	17	8	1
Controls	27	11	0	5	3	2	2	6	9	3	
Grand Total	83	47	1	13	12	5	17	23	26	11	1

*Discrepancy between total numbers in the various tables is due to cases omitted because of incomplete data or of other difficulties.

TABLE II

DEGREE OF PREMATURITY

CLASS	I	II	III	IV	CONTROL
No. of cases	13	53	30	6	39
Relation of P-P′ to P-P interval per cent*	64.4	61.4	56.6	48.2	66.0

*P-P′ is interval between normal auricular complex and the premature auricular deflection; P-P is the normal time interval between beats.

TABLE III

RELATIONSHIP OF P′R′ TO PR INTERVALS

CLASS	I	II	III	IV	CONTROL
No of cases	16	48	27	6	40
P′R′ interval in P.B.					
Longer than normal PR	1	10	11	2	4
Shorter than normal PR	7	20	5	1	12
Equal to normal PR	8	18	11	3	24

TABLE IV

HEART RATE

CLASS	I	II	III	IV	CONTROL
No. of cases	16	55	30	6	40
Average rate	94.0	88.3	92.3	82.0	90

records show auricular paroxysms with intraventricular block during the paroxysm in October, 1925. In April, 1928, the patient's gall bladder was removed and he appears to be doing fairly well in respect to his heart, although he has developed permanent block and auricular fibrillation. A third case, a man aged thirty-one years (diagnosis auricular and ventricular premature beats, paroxysmal tachycardia),

showed slight aberration in the course of paroxysms of tachycardia in October, 1914, more definite aberration under the same conditions in 1924. In March, 1928, he was perfectly well except for occasional extrasystoles. The fourth patient, a man twenty-seven years old, first showed paroxysmal auricular tachycardia with aberrant responses in January, 1919. He was well and working as a meat cutter in November, 1927, having since, however, shown a paroxysm of ventricular origin.

In Table III we have tabulated the different classes according to the relation of P′R′ to PR, whether longer, shorter, or equal. It

TABLE V

Q-T INTERVAL OF PREMATURE BEAT COMPARED TO THAT OF NORMAL BEATS IN THE SAME TRACING

CLASS	I	II	III	IV	CONTROL
No of cases	15	51	27	6	36
QT Shortening	9	26	14	2	16
QT Lengthening	1	7	6	2	0
QT Unchanged	5	18	7	2	20

TABLE VI

FOLLOW-UP DATA

CLASS	NUMBER FOLLOWED	LIVING	DEAD
I	12	8	4
II	21	9	12
III	6	3	3
IV	3	2	1
Control	21	11	10

appears, as might be expected, that the later in diastole the premature beat falls the less likely is the P-R interval of the premature beat to be prolonged. The fact that a considerable number of the P-R intervals in the case of the premature beats are shorter than the P-R intervals of the normal beats probably represents a position of the new ectopic auricular pacemaker nearer the A-V node than is the normal sino-auricular pacemaker.

The average rate of the heart in each class (Table IV) does not appear to be especially important in this connection. The significance of premature beats occurring with rapid heart rates will be the subject of a later communication from this laboratory.

In Table V we have given the data on changes of the Q-T interval (i.e., from the beginning of Q to the end of T) in premature beats. This interval represents the duration of ventricular systole. Shortening of the Q-T interval occurs more often with the aberrant responses. Shortening of systole is the common finding with increased heart rates normally and would be expected to be of frequent occurrence in the case of auricular premature beats, as we have found it to be.

Associated changes in the electrocardiogram, other than changes in the premature beat, were of no especial significance except that the series of records with aberrant auricular premature beats showed more T-wave abnormalities and a higher incidence of axis deviations than did the control series.

The number and variety of primary diagnoses represented in the series make it difficult to draw any conclusions, but we have found no significant difference in the gravity of the patient's condition as indicated by the diagnosis in the cases making up the different classes and control series. For instance, among the miscellaneous cases without heart disease are included lobar pneumonia, lupus vulgaris, acne vulgaris, tenia saginata, gall bladder disease, xeroderma, psychoneurosis, and duodenal ulcer. A definite diagnosis of heart disease was made 8 times in Class I (16 cases; 50 per cent); 19 times in Class II (55 cases; 34 per cent); 6 times in Class III (30 cases; 20 per cent); once in Class IV (6 cases; 16 per cent); and 16 times among 40 control cases (40 per cent).

Finally, in Table VI may be found the cases which have been followed, with the number living and the number dead. So far as we are able to judge, the end-results in those cases showing aberrant ventricular responses to auricular premature beats are not other than may be expected from associated findings or different from any group of cases showing auricular premature beats with normal responses.

SUMMARY AND CONCLUSIONS

1. A study has been made at the Massachusetts General Hospital of three hundred and eighty-seven consecutive cases with electrocardiograms showing auricular premature beats. Of this number the one hundred and seven cases showing aberrant ventricular responses to these auricular premature beats (with normal response to normal auricular stimuli*) have been analyzed. A study has also been made of the electrocardiograms of seventy-three cases of auricular paroxysmal tachycardia.

2. Aberration and the degree of aberration (intraventricular block) in the ventricular response to an auricular premature beat have been found to depend upon the degree of prematurity and so far as we have been able to judge the finding of aberrant ventricular responses to auricular premature beats does not alter appreciably the prognosis in a given case.

3. Aberration in the ventricular complexes during the height of a paroxysm of auricular tachycardia appears not to be serious, judging from a review of four such cases found among a total of seventy-three patients with auricular paroxysmal tachycardia studied by us.

*Except for a few cases which showed constant intraventricular block with increased aberration following auricular premature beats.

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THE POSITIVE CENTRIFUGAL VENOUS PULSE*

A Clinicopathological Correlation

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In 1925 Kerr and Warren[1] reviewed the literature on the peripheral venous pulsations and added valuable evidence of their clinical importance in the diagnosis of tricuspid insufficiency. The following year occasion was taken to report a new expedient in demonstrating the positive centrifugal venous pulse in the peripheral veins, namely, elevation of the forearm to a distance above the heart equivalent to the venous pressure.[2] This procedure simply serves the purpose of overcoming hydrostatic pressure to the end that such waves as are initiated in the great venous trunks on right ventricular contraction in the presence of incompetency of the tricuspid valve, are better transmitted peripherally. Otherwise the force necessary to overcome the inertia of the column of returning blood may dissipate the feeble centrifugal venous waves. These observations strictly confirmed the studies of Kerr and Warren in attributing a virtual pathognomonic value to this sign in tricuspid insufficiency.

Three of the cases reported in that communication came to necropsy and the measurements of the circumference of the tricuspid orifices (12, 12, and 13.5 cm. respectively) suggested an objective proof of the accuracy of the above conclusion. Since that time 12 patients with congestive heart failure showing the positive centrifugal venous pulse during life have died. The data relative to the pertinent clinical and pathological findings are tabulated below:

The range of measurement of the circumference of the tricuspid orifice was from 11.5 to 16.5 cm. with an average of 13.5 cm. Vierordt[3] gives 12 cm. as the normal figure for the circumference of the tricuspid orifice in the female and 12.2 (Wulff) to 12.7 cm. in the male. While these figures are deemed too high by certain pathologists, still they may serve in the present relation. Clearly 2 of 3 female subjects showed tricuspid measurements above the standard for their sex, while 8 of 9 males exceeded the above stated normal. In any event the majority of cases in this small series, showing a positive centrifugal venous pulse, had actual widening (relative insufficiency) of the tricuspid orifice at necropsy, and it is not necessary in such cases to invoke the second explanation of relative insufficiency, namely, the traction of the chordae

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TABLE I

DATA ON CASES OF DECOMPENSATION

NO.	AGE	SEX	CLINICAL DIAGNOSIS	POSITIVE CENTRIFUGAL VENOUS PULSE	CIRCUMFERENCE OF TRICUSPID ORIFICE (CM.)	HISTOLOGY—MYOCARDIUM
1	52	M	Myocardial degeneration; auricular fibrillation; relative tricuspid and mitral insufficiency.	+	14.6	Perivascular and interstitial fibrosis; hypertrophy.
2	75	M	Arteriosclerosis; myocardial degeneration; cardiac hypertrophy and dilatation; auricular fibrillation; relative mitral and tricuspid insufficiency.	+	13.0	Sclerosis of vessels; fibrosis; hypertrophy.
3	16	F	Rheumatic endocarditis (aortic and mitral) and pericarditis; myocardial degeneration.	+	12.5	Hypertrophy; fibrosis; necrosis; Aschoff bodies.
4	44	M	Chronic endocarditis (aortic and mitral); acute pericarditis; cardiac hypertrophy; myocardial degeneration; relative tricuspid insufficiency.	+	15.5	Hypertrophy; fragmentation; scars.
5	40	M	Tertiary syphilis; aortitis with aneurysm; aortic insufficiency; cardiac hypertrophy and dilatation; relative tricuspid insufficiency.	+	14.0	Anemic infarction with scarring; interstitial fibrosis.
6	32	F	Adhesive pericarditis; myocardial degeneration; relative tricuspid insufficiency.	+	11.5	Hyalin necrosis; atrophy
7	86	M	Arteriosclerosis; myocardial degeneration; auricular fibrillation.	+	11.5	Fibrosis; hypertrophy; perivascular lymphoid infiltration.
8	78	M	Arteriosclerosis; hypertension; myocardial degeneration; auricular fibrillation; cardiac hypertrophy.	+	13.0	Anemic infarcts; hypertrophy; scars.
9	62	M	Arteriosclerosis; hypertension; cardiac hypertrophy; myocardial degeneration; auricular fibrillation; relative tricuspid insufficiency.	+	13.5	
10	74	M	Arteriosclerosis; hypertension; cardiac hypertrophy; myocardial degeneration; relative mitral and tricuspid insufficiency.	+	14.0	Hypertrophy; necrosis; nuclei vacuolated, or absent in places.
11	68	F	Chronic endocarditis (mitral); cardiac hypertrophy and dilatation; myocardial degeneration; relative tricuspid insufficiency.	+	12.5	Fibrosis; hypertrophy; edema.
12	63	M	Toxic adenoma of thyroid; myocardial degeneration; cardiac hypertrophy and dilatation; auricular fibrillation; relative mitral and tricuspid insufficiency.	+	16.5	Hypertrophy; fibrosis; lipochromatosis.

tendineae on the valve margin through right ventricular stretch. The converse is not true. Absence of a positive centrifugal venous pulse does not rule out tricuspid insufficiency, since in a control group of 12 cases of congestive heart failure without this sign coming to necropsy in the same period of time, 8 showed tricuspid measurements exceeding the standard figures for their respective sexes. This failure to demonstrate the positive centrifugal venous pulse in the presence of anatomical insufficiency of the tricuspid valve may be explained by local edema in the arms, technical difficulties in observing minor venous waves, unusual integrity of the valves of the veins, right ventricular contractions too feeble to propagate waves into the peripheral veins or absence of residual blood in the right auricle.

A word of explanation is necessary with regard to the last mentioned point. Mackenzie on repeated occasions[4, 5, 6] remarked the necessity for a residuum of blood in the right auricle through which the regurgitant blood from the right ventricle might act, before venous pulse waves could be anticipated in the peripheral bed. "That [the ventricular form of venous pulse] is a sign of tricuspid regurgitation there is no doubt, but it is a sign of far greater significance, namely that the auricle does not precede the ventricle in the cardiac cycle."[6] Obviously from a mechanical or hemodynamic standpoint no circumstance would favor this situation more effectively than auricular fibrillation. Only 6 of the reported group of 12 cases of decompensation with a positive centrifugal venous pulse, coming to necropsy, had shown auricular fibrillation. Hence the phenomenon may occur in the absence of auricular fibrillation, provided the other factors for the production and propagation of the retrograde venous wave be present.

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STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATION OF HEART DISEASE

III. Heart Disease in Children*

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INTRODUCTION

THE wider interest in heart disease as a public health problem has in the past few years stimulated a renewed and intense interest in the etiology, pathology, and natural history of heart disease in children, particularly in that of the rheumatic variety. Cohn[1] in a recent issue of this journal has reviewed in detail published data bearing on the subject. He indicates the inadequacy of the information at present available and suggests the collection of data in a uniform manner so that necessary and more accurate information on the important phases of the problem may be obtained.

In this investigation an attempt was made to collate some basic data concerning the natural history of heart disease in children. The study is based on the statistical analysis of the case histories‡ of five hundred children observed in a clinic under the same medical supervision during a period of ten years. It presents data of interest on some of the problems of heart disease during the period ranging from childhood to adolescence. Of particular importance is the information obtained on the natural history of rheumatic infection in its relation to heart disease.

A consideration of data collected from clinical history records must always take into account obvious factors of error. In this investigation every effort was made to reduce these to a minimum. The medical supervision was uniform and the records were taken on special charts by trained workers. A number of children were observed from birth in the general clinic and about 150 were observed daily in special classes in school for a period of years.

Period of Observation.—The investigation covers a period of ten years (1916-1927). An attempt was made to obtain a final record of every patient living in 1927 (Table I). This was possible in all but

*Paper I. From the Department of Pediatrics, Cornell University Medical College, the Heart Clinic of the New York Nursery and Child's Hospital and the Committee on Research of the Heart Committee of the New York Tuberculosis and Health Association.

†Working on behalf of the Committee on Research of the Heart Committee, New York Tuberculosis and Health Association.

‡The clinical charts recommended by the New York Heart Committee described in a recent issue of this journal have been used since 1923. All the old records were transcribed to these forms. The use of these charts has made this statistical analysis possible.

17 per cent of the patients, who were not located. During the period of observation 10.8 per cent of the patients died. In 72.2 per cent a final record was obtained, so that in 83 per cent a complete record of the course of the disease to death or to 1927 was secured. Sixty-one and six-tenths per cent of the children were under continuous observation for a period less than three years and 38.3 per cent over a period ranging from three to ten years.

Age Distribution.—The ages ranged from infancy to twenty-two years. On admission, 12 per cent of the children were under six years of age and 50 per cent were from six to ten years of age. On final observation, 38 per cent were from eleven to fourteen years and 25 per cent from fifteen to twenty-two years of age (Fig. 1).

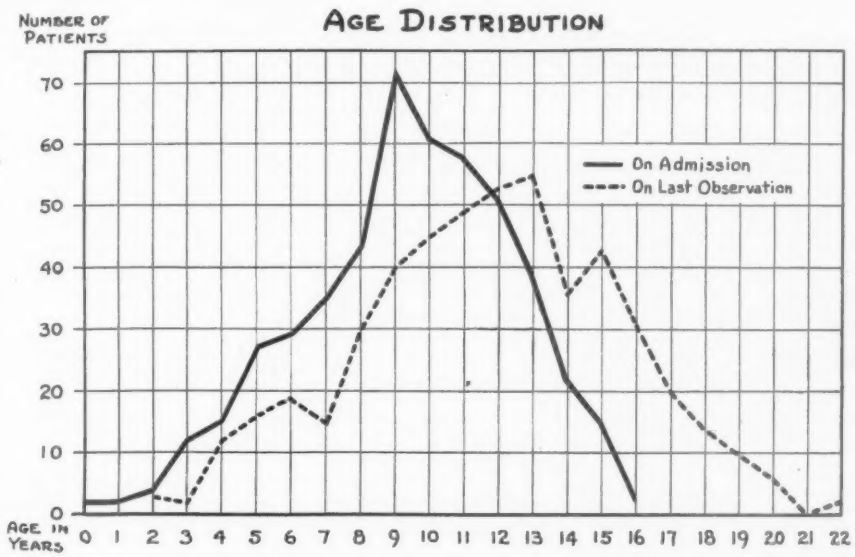


Fig. 1.

Etiology and Sex Distribution.—On first observation twenty-five children were classified as harboring possible heart disease (that is to say, there were negative histories, slight heart enlargement and persistent systolic murmur in the second to fourth left interspace—Class E). Of these children, twenty retained the same physical signs over the period of observation (Table II). This group is small in this series but it is representative of a large group which was under observation but is not included in this report. These children are also representative of cases with so-called inorganic or functional murmurs which are found in the course of school examination and form about one-half percent of the reported cases of heart disease in school children.[2] It is suggested that these childern may have some minor congenital malformation responsible for the persistent physical signs.

TABLE I

ETIOLOGY AND DISPOSITION OF CASE

ETIOLOGY (FINAL OBSERVATION)	% OF TOTAL CASES	TOTAL		UNDER CONTINUOUS OBSERVATION		DIED		INACTIVE					
								RETURNED FOR EXAMINATION		REPORTED ON		NOT LOCATED	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Rheumatic	79.0	395	100	187	47.3	47	11.9	47	11.9	57	14.4	57	14.4
Unknown	5.4	27	100	6	22.2	2	7.4	4	14.8	8	29.7	7	25.9
Class E	4.2	21	100	4	19.0	1	4.8	3	14.3	7	33.3	6	28.6
Congenital and Rheumatic	3.6	18	100	8	44.4	3	16.7	1	5.6	2	11.1	4	22.2
Congenital	7.6	38	100	16	42.1	1	2.6	5	13.2	5	13.2	11	28.9
Bacterial	0.2	1	100										
Total	100.0	500	100	221	44.2	54	10.8	60	12.0	80	16.0	85	17.0

Twenty-seven patients presented definite organic heart disease of unknown etiology (Table I). It is possible that they may have been rheumatic, but there was no evidence of any manifestation of rheumatic infection during the period of observation. It is suggested that heart disease in these children may be the result of some unknown or unrecognizable infection in infancy.[3]

Fifty-six, or 11.2 per cent, of the children were cases with congenital heart defect. Eighteen, or 3.6 per cent, of these also gave a complicating rheumatic history (Table I). Five had brothers and sisters with congenital heart defects. This incidence of 11.2 per cent may be considered as representative of the usual ratio of cases of congenital heart disease to the total number of cases of heart disease in children over the age of two years. Infants under two years with congenital heart defects were not included in this report.* The diagnosis of the particular congenital malformation is difficult to make and unreliable, since various cardiac malformations have been found at autopsy in cases that presented identical physical signs.† In 5 children the defect was recognized in the first year of life; in 12, between the second and the fifth year, and in the remaining 39 between the sixth and the thirteenth year. Forty-four children were well developed and in good general health. Four exhibited marked cyanosis, and in 8 general physical development was delayed. There were 4 deaths in this group, one from bronchopneumonia at the age of three years, and 3 from rheumatic heart disease at the ages of eight, sixteen, and seventeen years respectively.

There was one patient with organic heart disease of known bacterial etiology. This patient was observed before and after infection with diphtheria; the attack was complicated by post-diphtheritic paralysis.

*The London School[1] report gives the incidence of congenital heart disease as 14 per cent of the total cases of organic heart disease and the Bristol School[5] reports an incidence of 11 per cent of a total of 202 cases of organic heart disease.

†Schloss, O. M. and Wilson, James: Congenital Heart Disease: Clinical and Pathological Studies, Am. Jour. Dis. Child, (to be published).

The heart remained definitely enlarged without clinical evidence of valvular disease. The patient was observed for eight years and at no time during that period showed any manifestation of rheumatic infection.

The remaining cases (395 or 79 per cent) presented a rheumatic history (Table I). Of these, three-quarters suffered from organic heart disease. This is in marked contrast to the incidence of heart involvement (29.8 per cent) noted in a series of 473 children observed

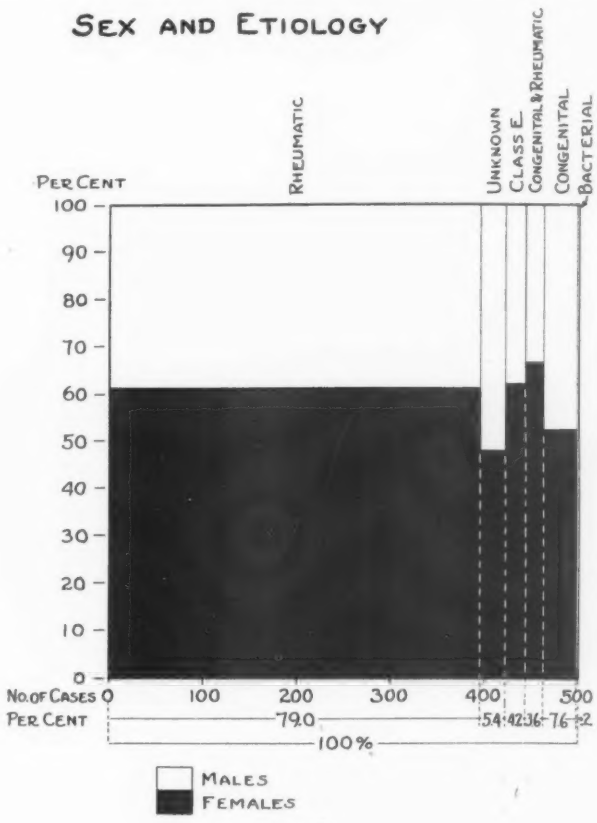


Fig. 2.

over a period of from two to six years at St. Thomas' Hospital.[9] The remaining were "potential" heart cases. This incidence confirms the general opinion that rheumatic infection is the most common etiological factor in heart disease in children. Recently, Wyckoff and Lingg[6] found from a statistical study of 1000 cases of organic heart disease that "in the second decade 80 per cent of the cases were of rheumatic etiology."

Correlation between sex and etiology shows for the total of 500 children a predominance of females (60 per cent females and 40 per

cent males). There was an almost equal sex distribution among children with heart disease of unknown etiology and congenital heart disease, whereas there was a predominance of females among those with rheumatic heart disease—61.2 per cent females as against 38.8

TABLE II.

RELATIVE DIAGNOSIS ON FIRST AND LAST OBSERVATION

FIRST OBSERVATION		LAST OBSERVATION DIAGNOSIS									
				CONGENITAL MALFORMATION							
DIAGNOSIS	% OF TOTAL	TOTAL		CONG. MALF. ONLY		CONG. MALF. & RHEUM. HIST.		CONG. MALF. & VALV. DISEASE		TOTAL	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Congenital Malformation only	8.4	42	100	36	85.8	4	9.5	2	4.7	42	100
Congenital Malformation and Rheum. History	1.6	8	100			6	75.0	2	25.0	8	100
Congenital Malformation and Valvular Disease	.8	4	100					4	100	4	100
TOTAL	10.8	54	100	36	66.8	10	18.5	8	14.7	54	100
Mitral Insufficiency	31.5	157	100								
Mitral Insufficiency											
Mitral Stenosis	17.0	85	100								
Mitral Insufficiency											
Aortic Insufficiency	1.0	5	100								
Mitral Insufficiency and Stenosis											
Aortic Insufficiency	2.4	12	100								
TOTAL	51.9	259	100								
Acute Rheum. Carditis	.6	3	100								
Possible Heart Disease (Class E)	5.0	25	100	2	8.0					2	8.0
Negative Heart	14.4	72	100								
Systolic Murmur	2.2	11	100								
Enlargement of Heart	11.9	60	100								
Systolic Murmur and Enlargement	3.2	16	100								
TOTAL	31.7	159	100								
TOTAL		500	100	38	7.6	10	2.0	8	1.6	56	11.2

per cent males (Fig. 2). This is in accord with the experience of other observers. The reason for it is at the present time unknown.

THE NATURAL HISTORY OF RHEUMATIC INFECTION IN ITS RELATION TO RHEUMATIC HEART DISEASE

*Social History.**—A consideration of social, environmental, and economic conditions in 329 cases of rheumatic etiology has suggested a study of certain matters which we wish to discuss in detail.

1. *Economic Status.*—The majority of the children came from moderately well-to-do homes of the industrial laboring class of the city. In 65 per cent of the cases the family budget was estimated as ade-

*Report from the Social Service Department of the New York Nursery and Child's Hospital.

quate to conditions for decent living ($1500.00 to $2600.00 per year). In 72 per cent the homes were clean. In 50 per cent they were neither overcrowded nor damp. It may be important to note that the location of about half of the homes was within three blocks (400 yards) of the Hudson river. Evidence of dampness was found in only 23 per cent of them. These data are in accord with those reported by the Medical

TABLE II—CONTINUED

RELATIVE DIAGNOSIS ON FIRST AND LAST OBSERVATION—CONTINUED

LAST OBSERVATION DIAGNOSIS																							
VALVULAR DISEASE										ACUTE RHEUM. CARDITIS		POSSIBLE HEART DISEASE (CLASS E)		POTENTIAL									
M. I.		M. S. M. I.		M. I. M. S. A. I.		M. I. A. I.		TOTAL						NEG. HEART		SYSTOLIC MURMUR		ENLARGEMENT		SYS. MUR. & ENL.		TOTAL	
NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
101	64.4	48	30.6	1	.6	2	1.2	152	96.8			1	0.6	2	1.3			2	1.3			4	2.6
		71	83 5			13	15.3	84	98.8									1	1.2			1	1.2
				4	80.0	1	20.0	5	100														
						12	100	12	100														
101	39.0	119	46.0	5	1.9	28	10.8	253	97.7			1	0.4	2	.8			3	1.1			5	1.9
1	33.3			1	33.3			2	66.6	1	33.3												
3	12.0							3	12.0			20	80.0										
21	29.2	5	6.9					26	36.1	2	2.7			24	33.3	1	1.4	13	18.1	6	8.3	44	61.1
5	45.4	1	9.1					6	54.5					1	9.1	4	36 4					5	45.5
21	35.0					1	1.6	22	36.6									29	48.3	9	15.0	38	63.3
4	25.0	1	6.2					5	31.2							1	6 2	1	6.2	9	56.3	11	68.7
51	32.1	7	4.4			1	0.6	59	37.1	2	1.3			25	15.7	6	3.8	43	27.0	24	15.1	98	61 6
156	31.2	126	25.2	6	1.2	29	5.8	317	63.4	3	0.6	21	4.2	27	5.4	6	1 2	46	9 2	24	4.8	103	20.6

Research Council in *Social Conditions and Acute Rheumatism*, in which "the greatest incidence of rheumatism was found in the better class of industrial homes." The report of the Housing Inquiry showed "a slightly more frequent dampness in the houses of rheumatic families and suggested proximity to waters and river courses as a possible factor. Overcrowding or extreme poverty were not prime factors, except as the resistance is lowered by unfavorable conditions of living.'"

2. *Race.*—Thirty-two per cent were of Irish stock; 19.5 per cent were American born; 12.5 per cent were Italian, and 4.1 per cent were Jewish. Only 18, or 4.6 per cent, of the children were colored, although

the clinic draws from a colored district.* The remainder were distributed among Germans, 8.8 per cent; Russians or Poles, 4.4 per cent, and others, totalling 13.5 per cent. The large proportion of Irish children should not be construed as necessarily indicating that this racial group is particularly susceptible to rheumatic infection, but rather as due to the fact that our clinic is situated in a section of the city that has a large Irish population.

3. *Physical Characteristics.*—A review of certain physical characteristics showed that 22.0 per cent of the children were of the brunette type, that is to say, had dark eyes and dark hair; 16.7 per cent of the blonde type, with blue eyes and light hair; 50.0 per cent of a mixed type, and but 2.9 per cent had red hair and blue eyes. The studies reported by St. Thomas' Hospital indicated that darker types tend to show a greater predisposition to rheumatism than the fairer types. This is at variance with the conclusion of Shrubsall that, at St. Bartholomew's Hospital, rheumatic affections show a special predilection for the pure blonde type.[7] This divergence in various reported series is probably related to the racial constitution of the groups studied. In our series the large number of children of mixed type seems to be accounted for by the large number of Irish and American children in our group.

4. *Heredity.*—Thirty-six per cent of the children had rheumatic brothers or sisters. In the St. Thomas' Hospital report,[9] a family incidence of rheumatism was obtained in 36.1 per cent and in Coombs' analysis,[10] an incidence of 50 per cent. St. Lawrence[11] found a family incidence of heart disease and acute rheumatic fever in 29 per cent and 24 per cent respectively; Faulkner and White[12] reported a family incidence of rheumatic affections in 8.8 per cent. The question of possible contagion in the families of the children in our series has been considered, but no direct evidence of such a factor was noted during the period of observation. The result of the British inquiry as to the element of contagion states our present view: "On the whole it cannot be said that there is in the facts collected any conclusive evidence of contagion though many of the facts are consistent with this view."

MANIFESTATIONS OF RHEUMATIC INFECTION†

An analysis was made of the records of 413‡ children who presented a rheumatic history. In their histories the following manifestations were regarded as evidence of the existence of rheumatic infection: polyarthritis, growing and joint pains, chorea, acute carditis, and sub-

*Wood, Jones, and Kimbrough[8] found that rheumatic heart disease "seemed to be less common among the colored people than the white people of Virginia." Unfortunately we could find no other direct observations recorded on this subject.

†The term Rheumatic Infection is used although it is appreciated that the evidence of its infectious nature is at present not conclusive.

‡This includes the 18 cases of congenital heart disease complicated by rheumatic infection.

cutaneous nodules. Tonsillitis was not included here as a manifestation of rheumatic infection because of the difficulty in differentiating, from a history between severe pharyngitis occurring with upper respiratory infections in young children, and frank tonsillitis assumed to be of a rheumatic nature. The occurrence of other manifestations, such as urticaria, purpura, and epistaxis, have likewise not been included.*

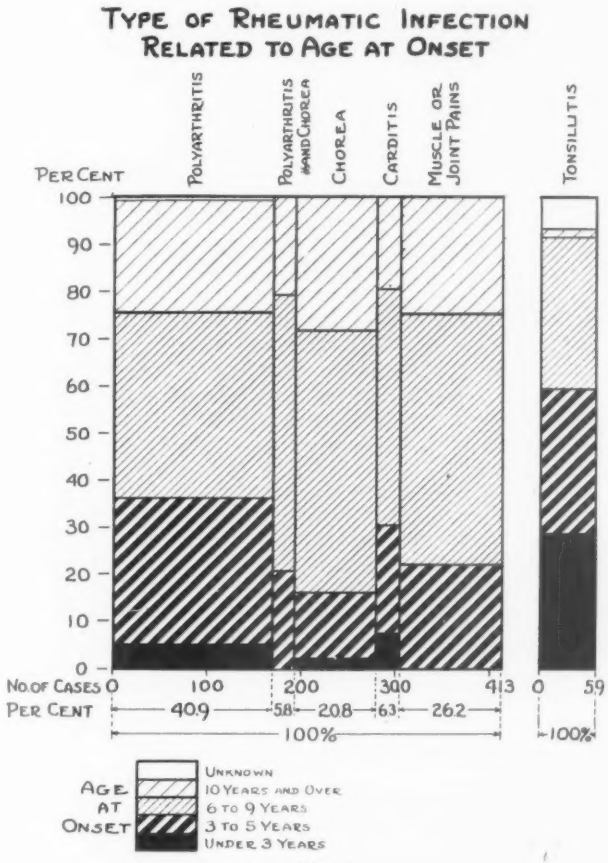


Fig. 3.

1. *Age at Onset.*—Before taking up the various manifestations of rheumatic infection we shall consider the clinical course of the disease, as a whole. It was found that, regardless of the particular kind of manifestation, the initial manifestation of infection occurred in the age group comprising the years six to nine, in about one-half of the cases (Fig. 3). In Mackie's[13] series the incidence curve of initial infection differs from this one in that it rises to a peak of 23.9 per cent in the group between the ages of six and nine years, 23.1 per

*In a previous publication an analysis of 185 case records shows various erythemas or skin lesions in 8 per cent and recurrent epistaxis in 11 per cent.

cent between ten and fifteen years and then slowly but progressively falls. It must be remembered, however, that Mackie's figures are not directly comparable with ours, in so far as our group is confined to children, whereas his includes adults. Histories obtained from adults are apt not to include the early complaints of childhood, which may account for the later dates of onset in Mackie's series. Ninety-eight and four-tenths per cent of our cases had their initial infection before they reached the age of fifteen, and almost 50 per cent of Mackie's cases had their first attack of rheumatic infection after the age of fifteen years was reached.

Fig. 4 shows the distribution of these 413 cases according to the age at which the first infection appeared. It may be seen that, begin-

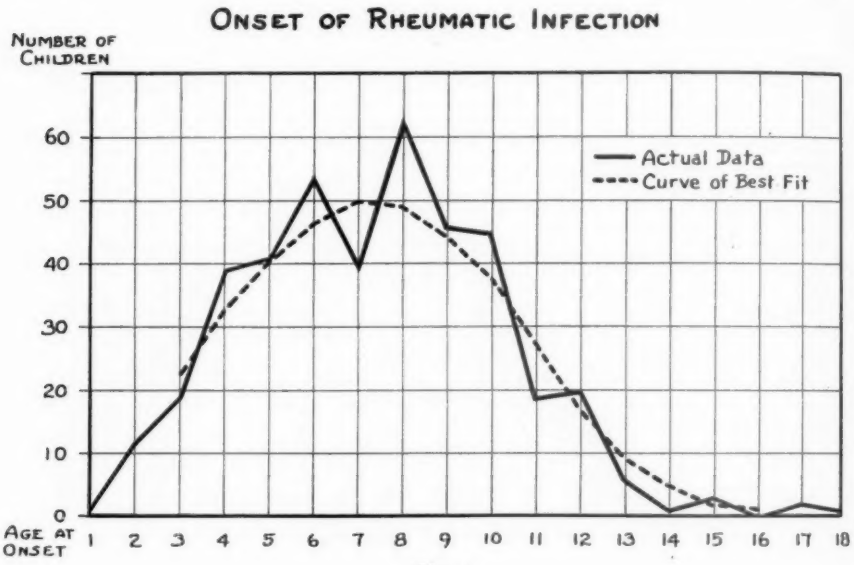


Fig. 4.

ning with the preschool ages, the curve gradually rises to the age of about six, remains high, up to the age of nine and declines thereafter. The average age at onset was found to be seven and three-tenths years, in comparison with an average of ten and two-tenths years reported by Cóombs,[10] and seven by Poynton[14] in similarly constituted series. It is important to note that our dating of the age of onset is in all probability accurate because about 50 per cent of the children came under our observation within a year of the onset of their rheumatic infection.

2. *Recurrence of Manifestations of Infection.*—Three hundred and two of 413 children in this group, or 73.0 per cent of the cases, suffered from one or more recurrences of infection (Fig. 5).* This figure must

*Mackie[13] found 71.5 per cent relapses in a series of 252 children, and in a group of 257 cases seen at St. Thomas' Hospital[9] there were 85.0 per cent relapses.

be regarded as a minimum. Attention has already been called to the varying length of time that these children were observed after the first attack of infection. Of the 111 children for whom no recurrence of infection is reported, 53.0 per cent were observed for less than three years after the initial episode, as against only 7.2 per cent observed for less than three years in the series of 302 children for whom relapses are reported. Obviously, before a statement can be

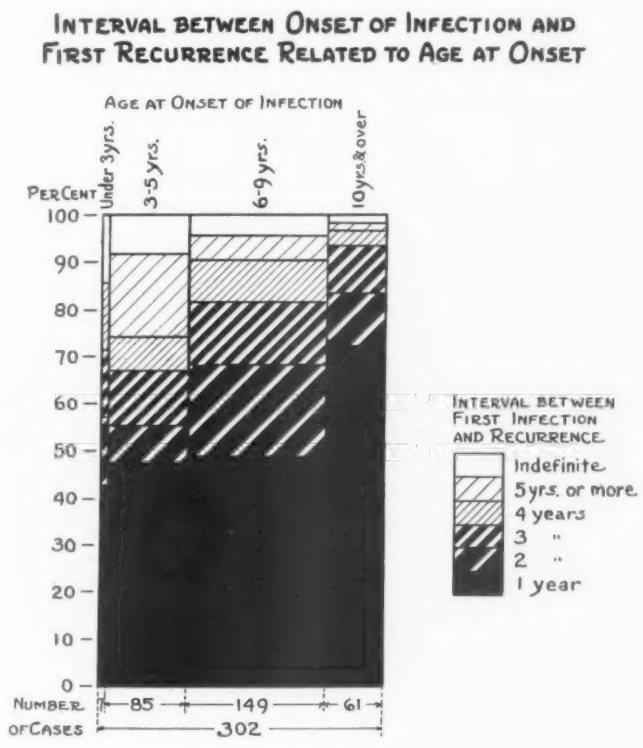


Fig. 5.

made as to the final fate of the 53.0 per cent (those observed less than three years), observation must extend over many more years.

3. *Recurrence of Infection and Age at Onset.*—Recurrences of manifestations of infection during the course of the disease appeared most frequently in the group of children who had acquired their initial infection at an early age. Eighty-five per cent of those who were afflicted between the ages of three and five suffered recurrences, as against 72.3 per cent in whom the initial infection occurred between the ages of six and nine, and 62.8 per cent among those in whom the infection began at ten years or over. Mackie reports the incidence rate of recurrence likewise highest in the group that experienced the

initial attack between the ages of five and ten years. In his series the disease recurred in 93.4 per cent.

4. *Interval Between Onset and Recurrence.*—An analysis of the interval which elapsed between the first noted manifestation of infection and the first recurrence shows that about half of the total cases relapsed within a year, two-thirds within two years, and four-fifths or 80 per cent within three years (Fig. 5). In only 15 per cent did at least four years elapse before the first recurrence of any manifestation of rheumatic infection appeared. There is here a striking difference between our experience and Mackie's, our 50 per cent as against his 23.6 per cent within the first year and our 15 per cent as against his 43 per cent after four or more years. The difference in the age constitution of the two series must again be taken into account. Only 1.4 per cent of our cases, but 48.9 per cent of Mackie's had reached the age of fifteen years or more, when the first rheumatic attack appeared. In our experience, recurrences are most frequent before this age is reached.

When related to the age at onset the greatest incidence of recurrence *within one year of onset* (72.2 per cent) was observed in children who were first infected at the age of ten or more years. This observation is of particular importance because 84 per cent of these children were between ten and twelve years of age, the age of puberty. It is possible that this is a critical age for children with rheumatic infection.

5. *Periods Free From Infection.*—Fig. 6* is a graphic description of the clinical course of the disease experienced by each child. The distribution of the cases† is arranged according to (1) the age at onset, (2) years in which there were manifestations of infection, and (3) the age reached at the time of last observation or report.

Even casual inspection of this chart impresses one with the apparent chronicity of the disease. To experience one, two, three, even four years of freedom from infection is not unusual, but even after longer periods relapses are frequent. Twenty-one children, for example, had 5 consecutive years of freedom from infection. Of these 8, or 38 per cent, relapsed at the end of that time. Thirteen were not under our observation for a longer period, but our experience leads us to expect relapses in some of these, if not in all. For instance, 17 children were free for six consecutive years, of whom 6 relapsed; 6 were free for seven years of whom 4 relapsed; 2 for nine years and one relapsed at the end of that period; of 4 who were free for ten or eleven years, one relapsed even after ten years.

*For the form of this chart we are indebted to Dr. John Wyckoff who used it in a paper, not yet published, a preliminary report of which was read at a meeting of the Pediatric Section, New York Academy of Medicine, Bulletin of the New York Academy of Medicine, 1926, Second Series, ii, No. 2.

†Case No. 413 was not included in this chart, because dates at which manifestations of infections appeared were not accurately given by child's parent.

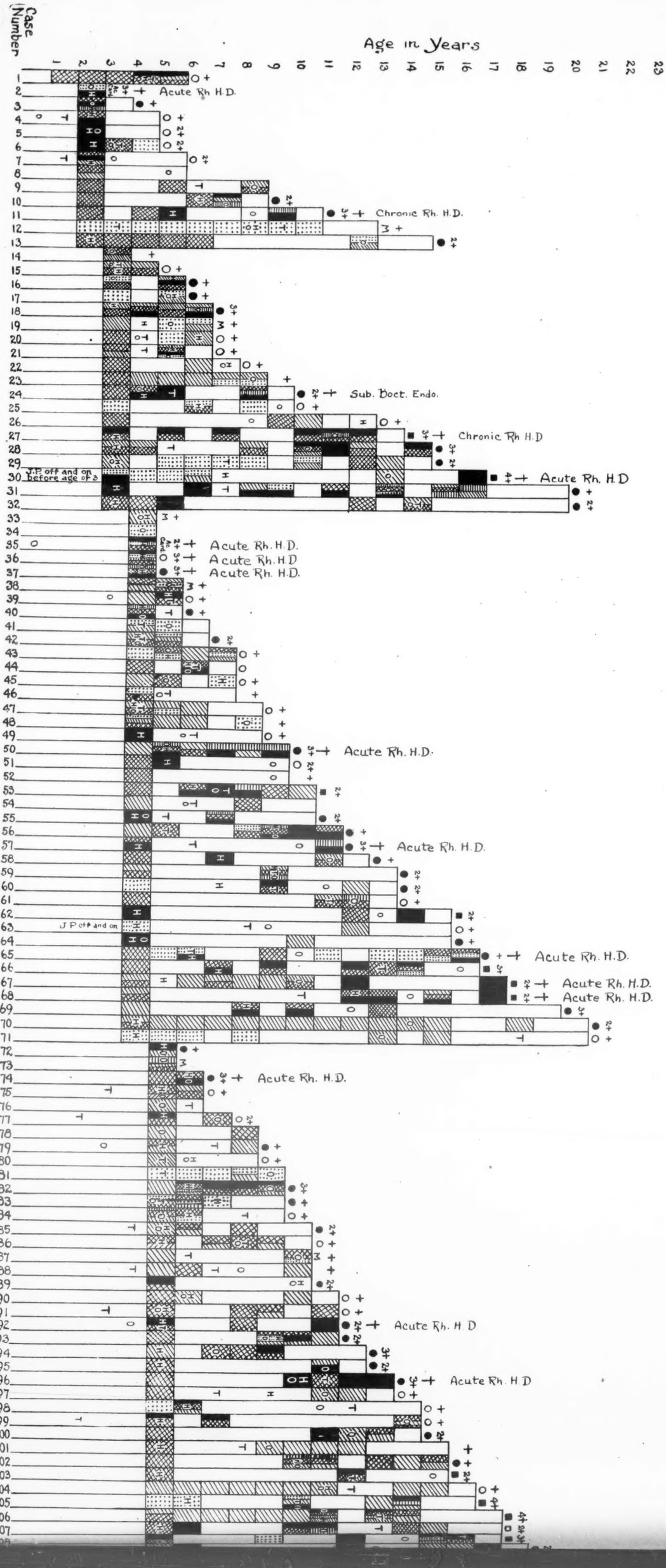
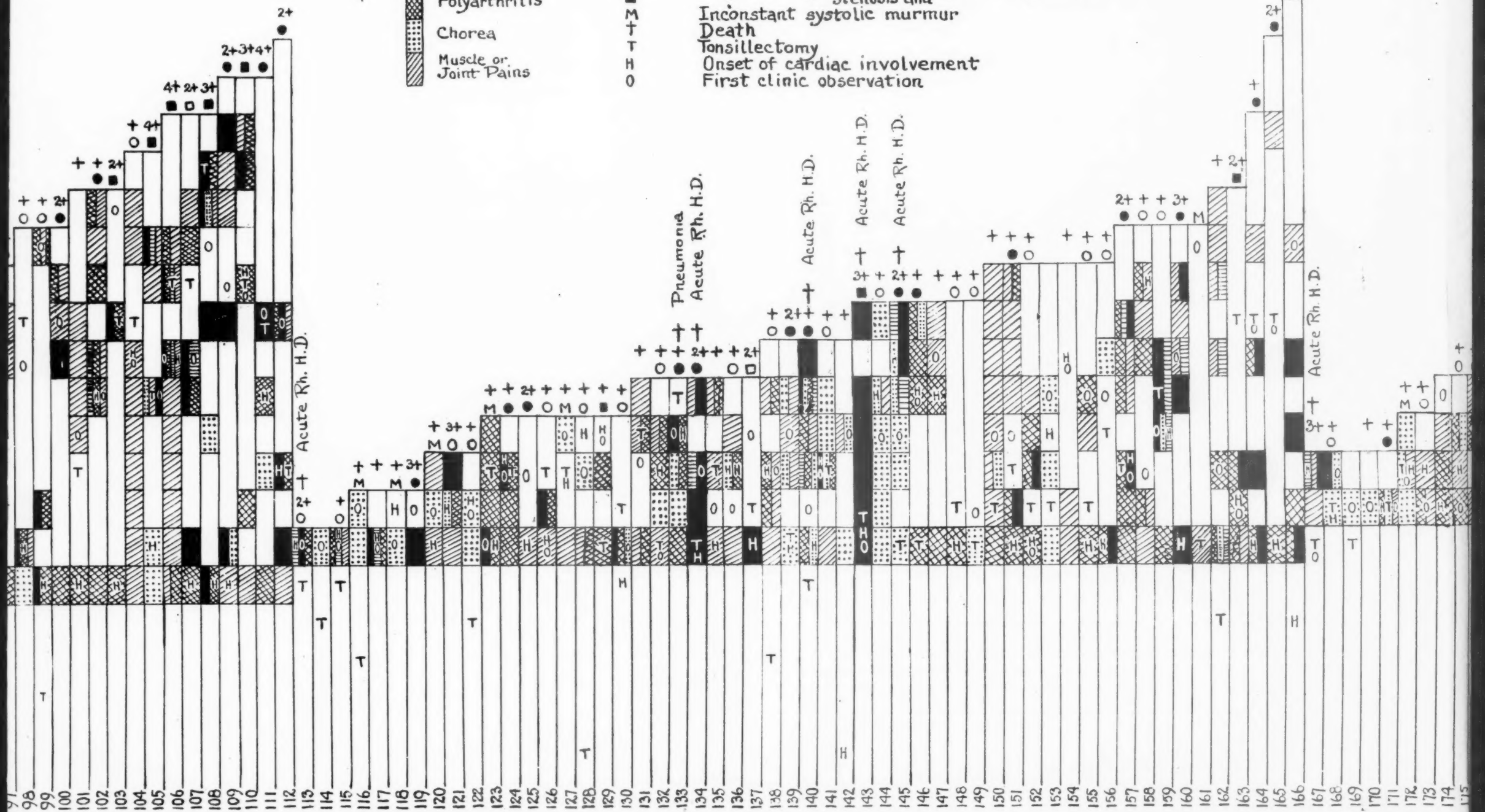
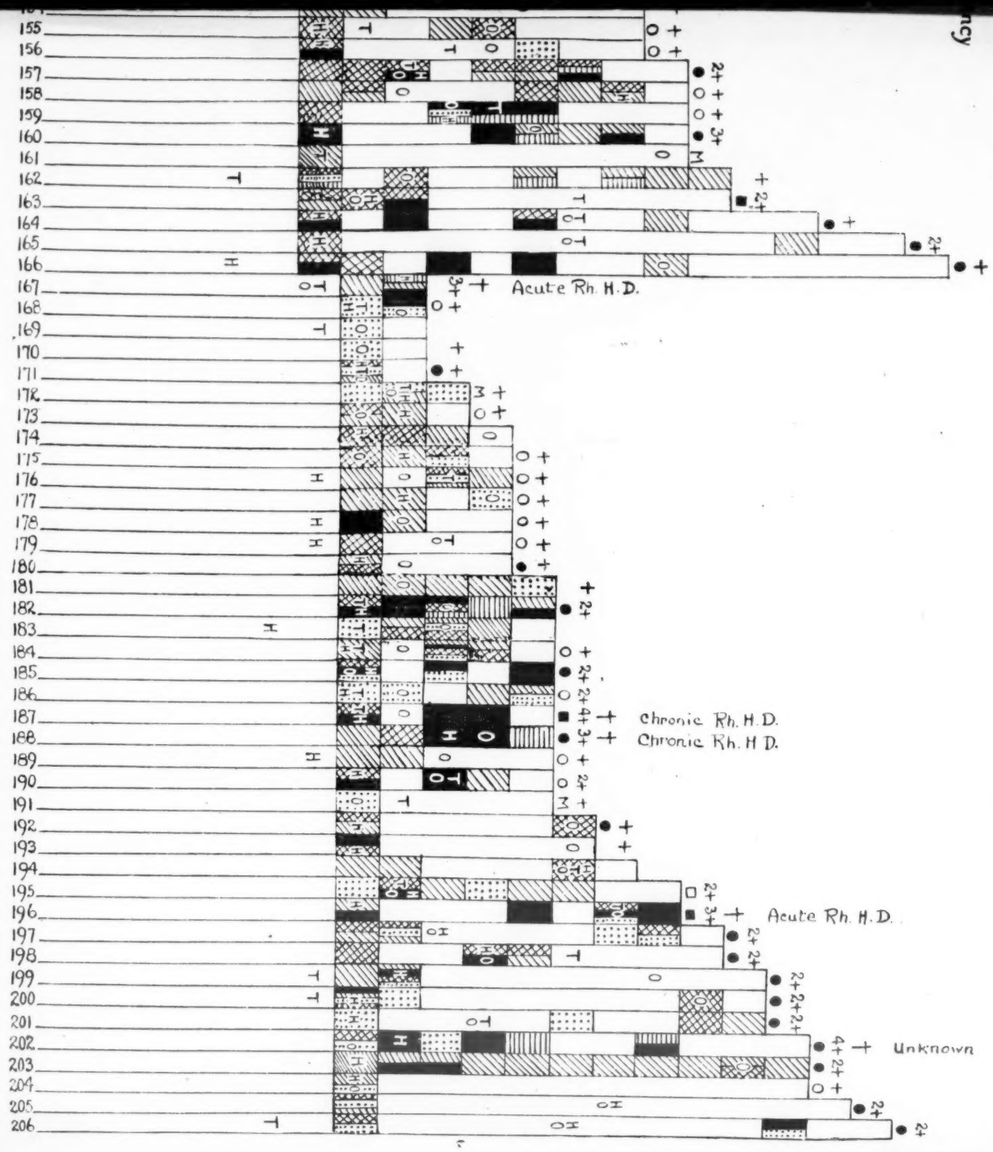

Case Number
Age in Years
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
Acute Rh H.D.
Chronic Rh. H.D.
Sub. Bact. Endo.
Chronic Rh H.D
J.P. off and on before age of 3
Acute Rh. H.D.
Acute Rh. H.D
Acute Rh. H.D.
Acute Rh. H.D.
Acute Rh. H.D.
J P off and on
Acute Rh. H.D.
Acute Rh. H.D.
Acute Rh. H.D.
Acute Rh. H.D.
Acute Rh. H D
Acute Rh. H D

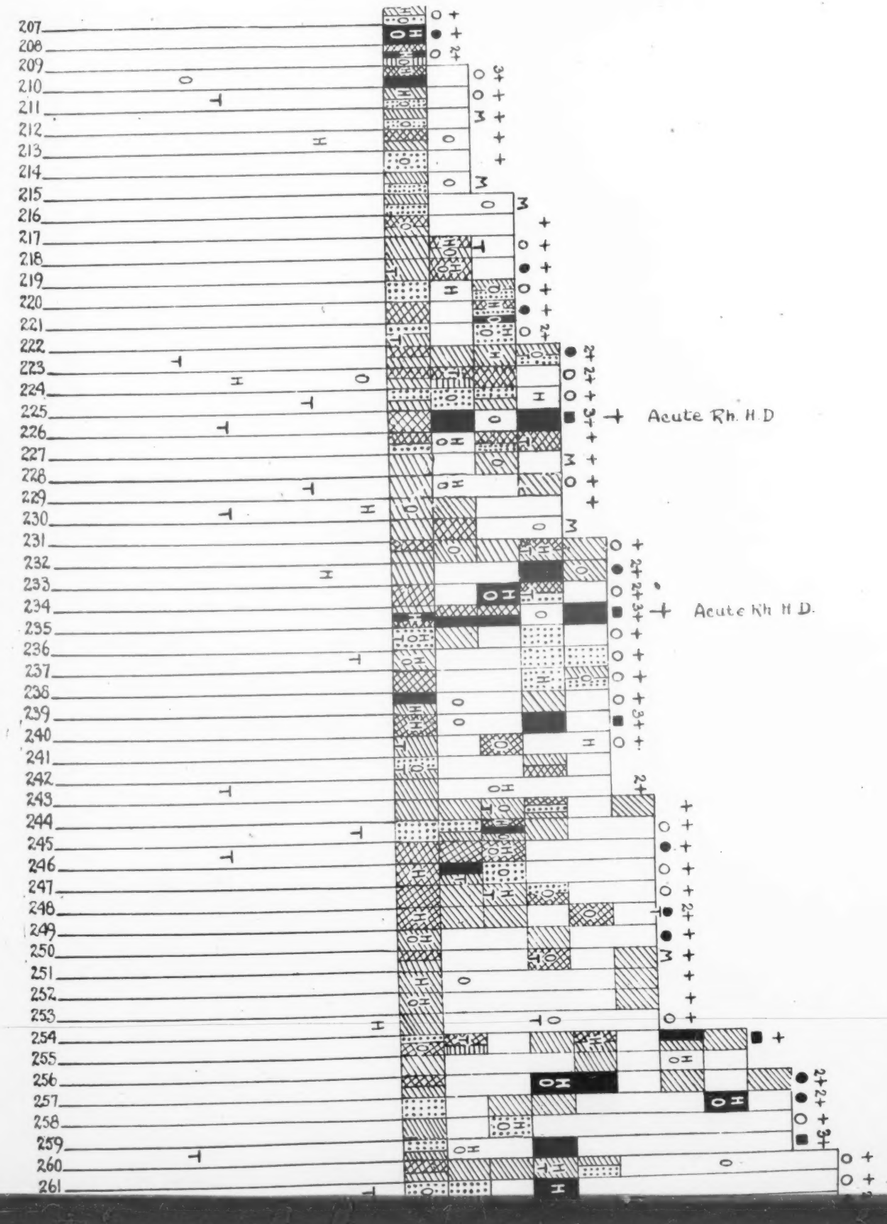
FIGURE VI KEY

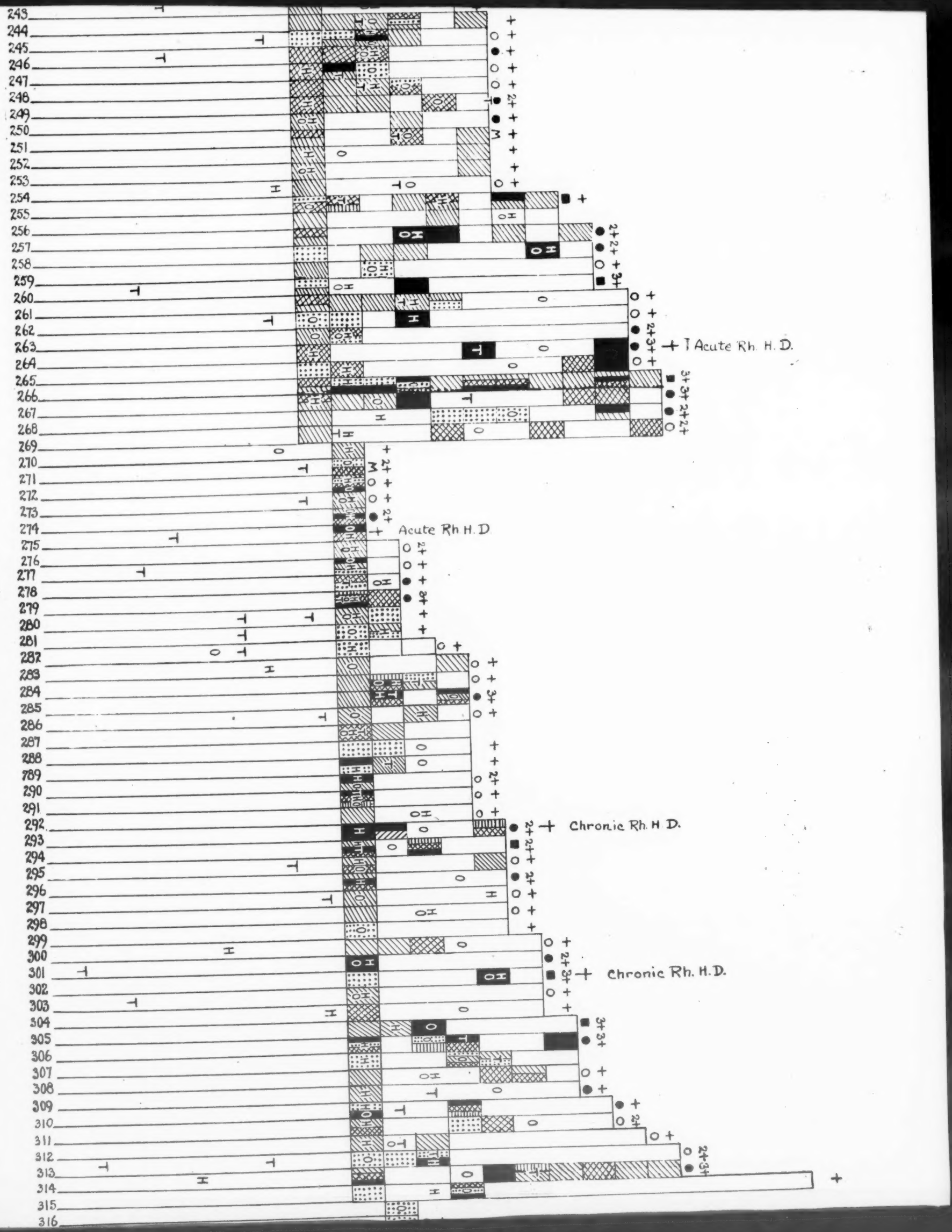
Acute Rheumatic Carditis
Nodules
Polyarthritis
Chorea
Muscle or Joint Pains

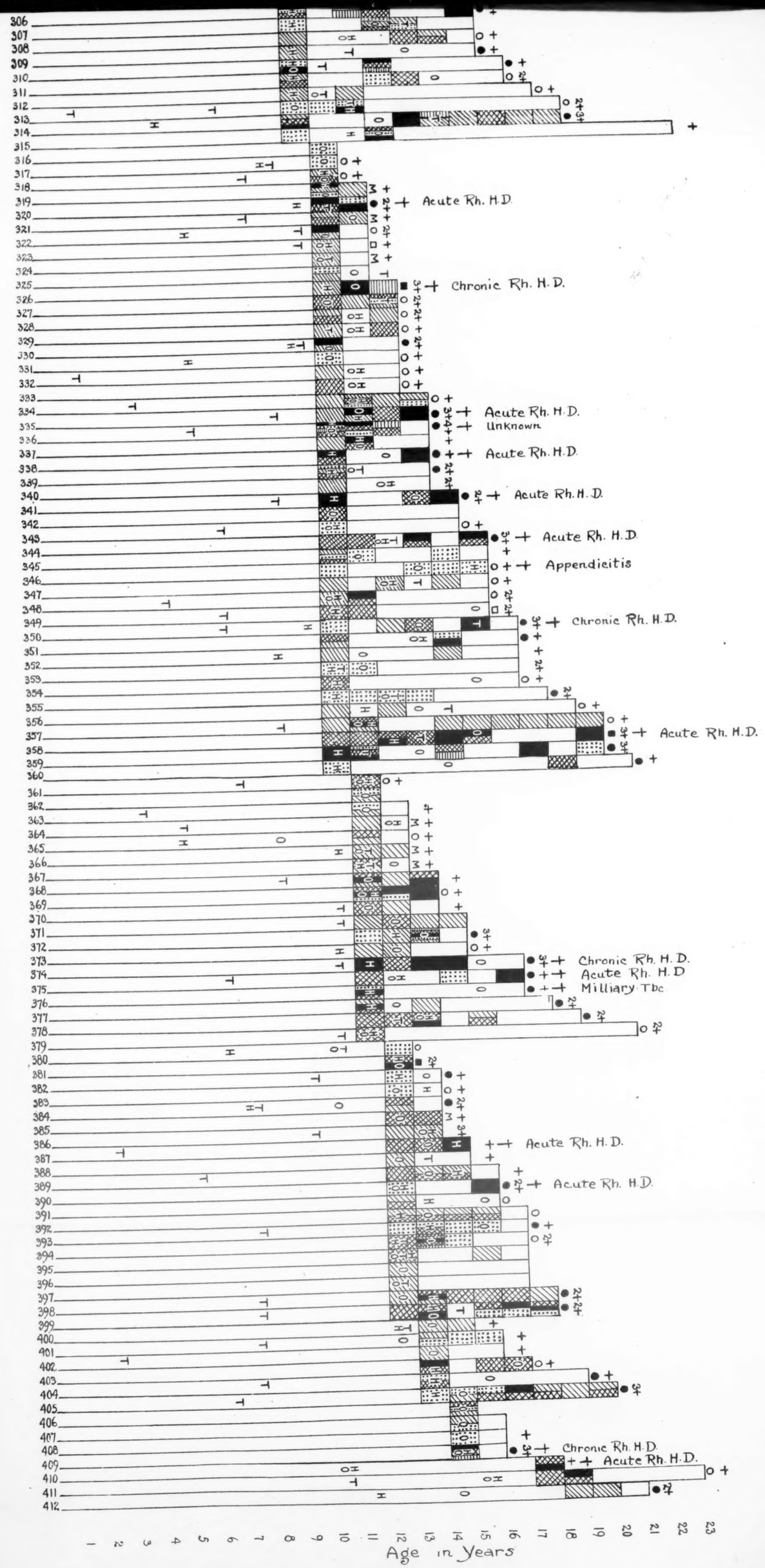
+, 2+, 3+ Degree of heart enlargement
○ Mitral insufficiency
● " " and stenosis
□ " " " aortic insufficiency
■ " " stenosis and " "
M Inconstant systolic murmur
† Death
T Tonsillectomy
H Onset of cardiac involvement
O First clinic observation




Acute Rh. H.D.
Chronic Rh. H.D.
Chronic Rh. H.D.
Acute Rh. H.D.
Unknown


Acute Rh. H D
Acute Rh H.D.


Acute Rh. H. D.
Acute Rh H. D
Chronic Rh. H. D.
Chronic Rh. H. D.


Acute Rh. H.D.
Chronic Rh. H.D.
Acute Rh. H.D.
Unknown
Acute Rh. H.D.
Acute Rh. H.D.
Acute Rh. H.D.
Appendicitis
Chronic Rh. H.D.
Acute Rh. H.D.
Chronic Rh. H.D.
Acute Rh. H.D
Milliary Tbc
Acute Rh. H.D.
Acute Rh. H.D.
Chronic Rh. H.D.
Acute Rh. H.D.
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
Age in Years

Certain detailed considerations disclosed by a study of this chart we desire to discuss.

6. *Age Susceptibility.*—An attempt was made to draw a frequency curve to determine the ages, provided they exist, at which rheumatic subjects are most susceptible to infection. It was found that the 413 children, together, experienced 1728 manifestations of infection, an average of four attacks per child. Because of the difficulty of defining a relapse or recurrence, that is to say, of deciding when one attack has ended and another has begun, it was thought best to present the data according to age at which manifestations of infection occurred, without attempting to determine whether, for instance, a child suffered one or more manifestations in a single year, or whether the second or third manifestation of infection might be but an exacerbation of the original attack. Presentation of the data in this manner shows that the 413 children together experienced 1140 years in which infection was present, an average of two and three-quarters years per child.

The curve showing the ages at which infection was present, when smoothed, appears nearly symmetrical, though somewhat skewed to the right, with a modal average at nine years (Fig. 7-*A*). The second half of this curve may not represent the facts as they really are because of the relatively small number of children included in this study who reached the upper ages, from nine to sixteen years. Consecutive curves were therefore drawn including data concerning children all of whom reached certain specific ages, as, nine years, ten years and so on, to eighteen. It should be noted from this series of curves that the modal average ranges from nine to twelve years. In every case the curve begins to descend at some point within these age limits. In general, all the curves which succeed it conform to the total frequency curve. The very small number of children that reached the ages of sixteen, seventeen and eighteen years may very likely be responsible for the apparent flatness of these curves to the right of the mode. In spite of the insufficient number of cases included in this series, the curves confirm the belief that rheumatic infection, in its various manifestations, concerns itself primarily with children of the grade school age; their plain meaning seems to be *that about or before the age of twelve, the tendency to infection begins to diminish.*

It seems to us to be of very great importance to point out the probability these curves show, that age may be a factor in judging the influence of any therapeutic measures on the natural course of the infection. The results of any therapeutic measure, such as tonsillectomy, prolonged convalescent care, or specific serum or vaccine therapy instituted before or after children have reached an age of from nine to twelve years, must be judged accordingly. In a subsequent communication a study of the influence of tonsillectomy will be presented in connection with this series of rheumatic children.

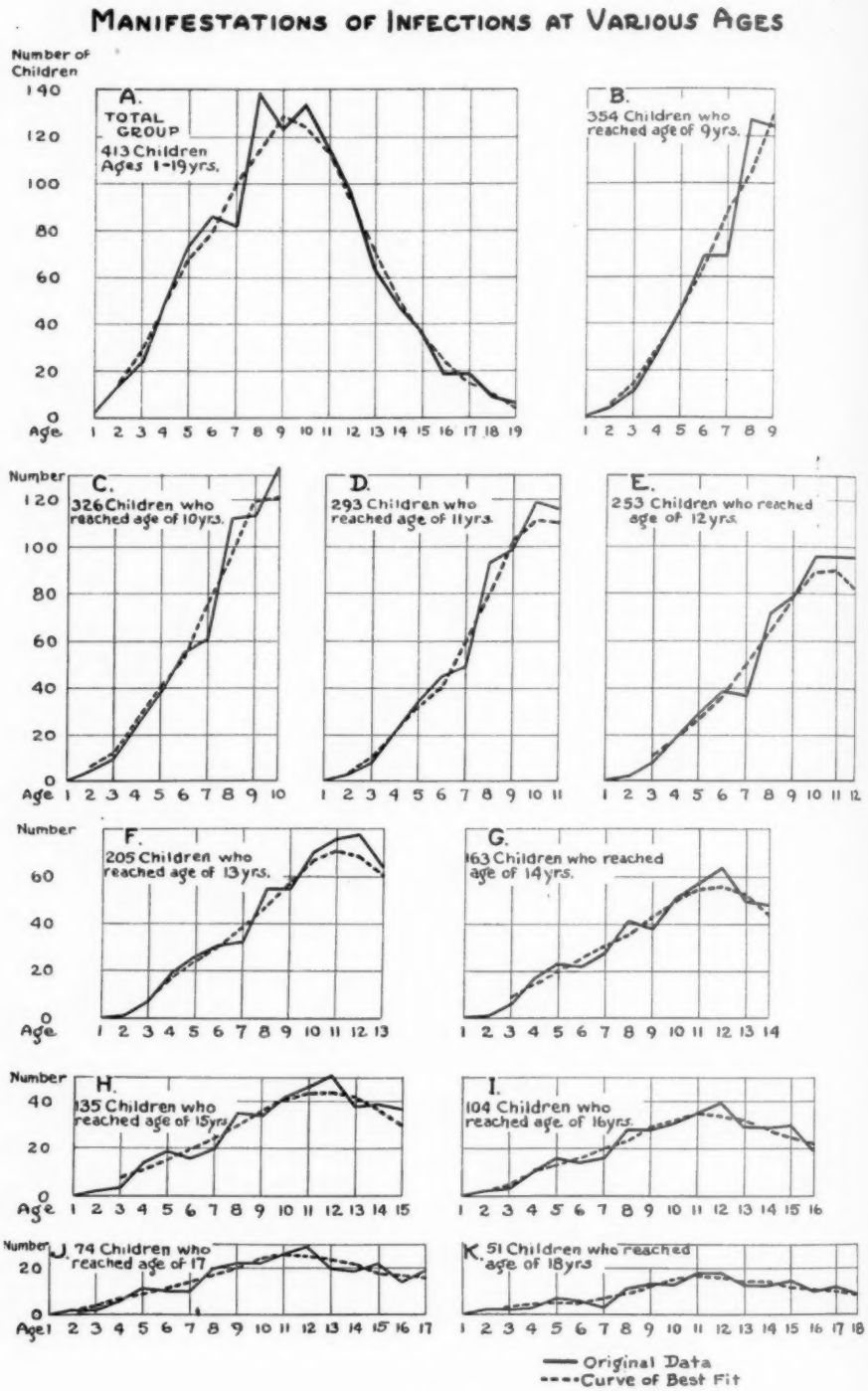

MANIFESTATIONS OF INFECTIONS AT VARIOUS AGES
Number of Children
A.
TOTAL GROUP
413 Children Ages 1-19 yrs.
B.
354 Children who reached age of 9 yrs.
C.
326 Children who reached age of 10 yrs.
D.
293 Children who reached age of 11 yrs.
E.
253 Children who reached age of 12 yrs.
F.
205 Children who reached age of 13 yrs.
G.
163 Children who reached age of 14 yrs.
H.
135 Children who reached age of 15 yrs.
I.
104 Children who reached age of 16 yrs.
J.
74 Children who reached age of 17
K.
51 Children who reached age of 18 yrs
Number
Age
Original Data
Curve of Best Fit

Fig. 7.

7. *Expectancy.*—Figures such as these, if they cover a large enough number of cases to satisfy the law of probability, should enable one to draw a curve which would show expectancy at each age; that is to say, would make possible prognostication as to whether a child is likely to have years free from infection immediately following a given age, and if so, how many such years may be expected to pass before a relapse takes place. We have attempted to draw such curves.

It appears, Fig. 8-*A*, that there is variation in the number of years that may occur free from infection. Our chart is to be read as follows: Of the 172 children who were infected at or before the age of seven years, 50 per cent relapsed in the eighth year, almost 20 per cent were free from infection in the eighth year, and then relapsed; the remaining 30 per cent were free in the eighth and ninth years, or longer, before relapse took place. Of those who were infected at or before the age of fifteen, however, only 34 per cent relapsed in the sixteenth year; 24 per cent were free in the sixteenth year, and then relapsed, and the remaining 42 per cent were free the sixteenth and seventeenth years, or longer, before relapse took place.

On the basis of this limited experience of 413 cases, one might say, then, that at the age of seven, the chances are even that a rheumatic child will undergo a recurrence the following year; of the children not likely to relapse the following year, the chances are two to three that the interval of freedom from infection will be not greater than one year. At the age of fifteen, however, the chances are only one to three that infection will recur in the following year; if no recurrence takes place at that time, the chances are about one to two that the interval of freedom from infection will be only one year.

The conclusion that can be drawn from this chart may be paraphrased also in this manner; of 172 children who have arrived at the age of seven years, and who have by this time become infected, only 6, or 3.5 per cent, in our experience can hope, in the years following, to remain free from infection for a period as long even as six years; only one for a period as long as ten years. Beyond this our observations do not yet reach.

The older the age group which is studied, the greater seems to be the chance of freedom from infection. At the age of twenty years about 75 per cent were free in the twenty-first year—that is to say, for the next year; and 25 per cent were free for three years, from ages twenty-one to twenty-four. Our records go no further. In comparison with age seven this is a gain, for of these only 50 per cent could hope for one free year, and only about 10 per cent for three such years.

In general, the curves indicate that, at any age before the age of seven, the chances are 3 to 5, or greater, that a rheumatic child will

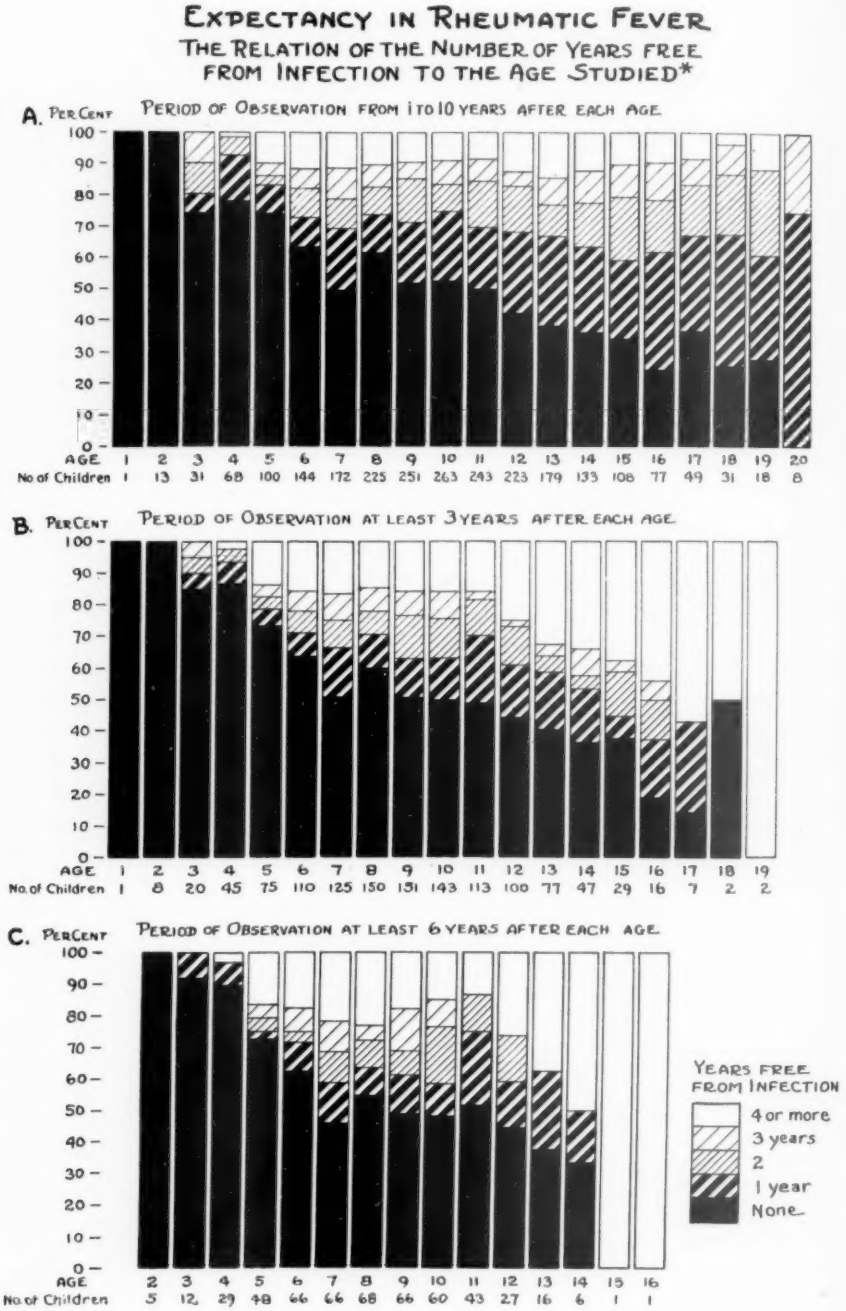

EXPECTANCY IN RHEUMATIC FEVER
THE RELATION OF THE NUMBER OF YEARS FREE FROM INFECTION TO THE AGE STUDIED*
A. PER CENT
PERIOD OF OBSERVATION FROM 1 TO 10 YEARS AFTER EACH AGE
100
90
80
70
60
50
40
30
20
10
0
AGE 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
No of Children 1 13 31 68 100 144 172 225 251 263 243 223 179 133 108 77 49 31 18 8
B. PER CENT
PERIOD OF OBSERVATION AT LEAST 3 YEARS AFTER EACH AGE
100
90
80
70
60
50
40
30
20
10
0
AGE 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Children 1 8 20 45 75 110 125 150 151 143 113 100 77 47 29 16 7 2 2
C. PER CENT
PERIOD OF OBSERVATION AT LEAST 6 YEARS AFTER EACH AGE
100
90
80
70
60
50
40
30
20
10
0
AGE 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
No of Children 5 12 29 48 66 66 68 66 60 43 27 16 6 1 1
YEARS FREE FROM INFECTION
4 or more
3 years
2
1 year
None

Fig. 8.

be subject to recurrent manifestations of infection the following year; at any age between the ages of seven and eleven, inclusive, the chances are about even, and at any age after the age of twelve, the chances are about 2 to 5, or less. Similarly, the number of consecutive years of freedom from infection tends to increase as the adolescent ages are reached.

It was thought that the fact of the varying number of years that children were observed after different ages might lead to erroneous conclusions. Data were tabulated therefore concerning only those

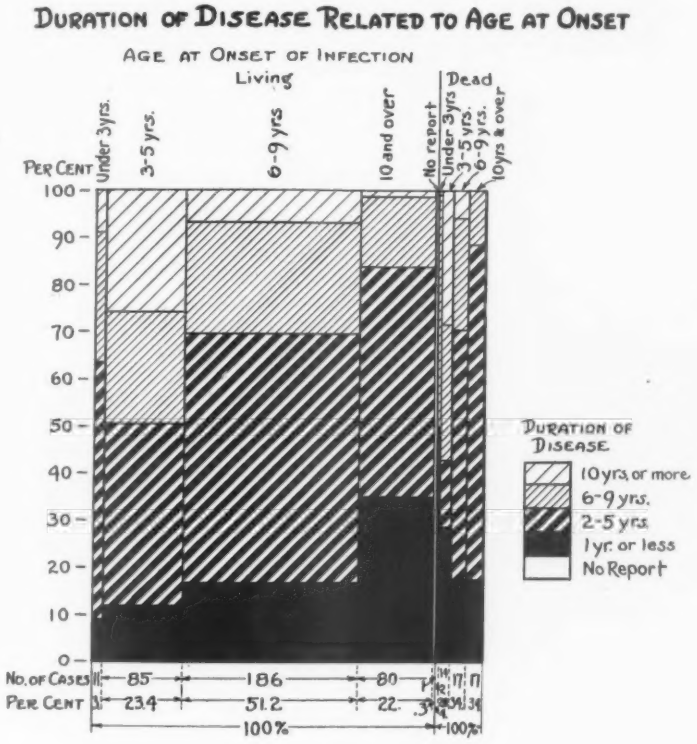


Fig. 9.

children who were observed three years or more (Fig. 8-*B*) or six years or more (Fig. 8-*C*), respectively, that is to say for periods not less than three or six years, after each age. In general, the picture remained the same.

Within recent years, efforts have been made to estimate the results of certain therapeutic measures. Among criteria suggested for making such judgments that of considering recurrences of manifestations of infection after therapeutic measures have been instituted has been emphasized, such therapeutic measures for instance as tonsillectomy or convalescent care. That such judgments cannot confidently be

made without relation to the natural course of the disease, especially without regard to recurrences, seems obvious in view of the data (Figs. 7 and 8) that have been presented.

It must be emphasized again that these curves are not presented as reliable expectancy curves, but merely as preliminary statements based on the facts which have emerged in studying this series of 413 rheumatic children. It is believed, however, that by concerted effort it may be possible later to draw reliable expectancy curves which will be valuable as a background against which to measure results of treatment.

8. *Duration of the Disease.*—Of the total 413 children, 46 per cent came under observation within one year of the onset of the first manifestation of infection. Three hundred and sixty-three, or 88 per cent, are living (Fig. 9). In 67.8 per cent of these the duration of the disease has been from one to five years, in 21.8 per cent from six to nine years, and in 10.2 per cent from ten to sixteen years. Fifty children, or 12 per cent died. Eleven, or 22 per cent, died within one year of the onset of infection. In 46 per cent the duration of the disease was from six to nine years, and in 10 per cent from ten to fifteen years.

9. *Prognosis.*—From the data presented, little of prognostic value could be learned. This may be due to the fact that the number of deaths is small, even though the mortality rate in the series is relatively high. When the age at death was compared with the age distribution of the living, it was found that no single age or age group claimed a predominatingly high mortality. Likewise, there appeared to be no relation between mortality and the duration of the disease. The age at onset, however, and the severity of a particular attack of infection appeared to influence the duration of the disease. The figures indicate that children infected before the age of five and after the age of ten have a somewhat less favorable prognosis than those infected in the intermediate ages.

10. *Causes of Death.*—In forty-four children, or 88 per cent of the deaths, the cause of death was rheumatic heart disease. Death followed acute rheumatic carditis in 34 of these. One child died of bacterial endocarditis, one of lobar pneumonia, one of suppurative appendicitis, one of miliary tuberculosis, and two of causes unknown. The most common age at death was between eleven and fourteen years. Forty-five per cent of the deaths occurred in this age group.

11. *Incidence of Measles and Scarlet Fever.*—The possible relation between susceptibility to rheumatic and to other infections was considered. Two hundred and twenty-two, or 53.7 per cent, of the rheumatic children presented a history of measles. In 36.9 per cent, measles occurred between the ages of three and five years (Table III).

Halsey[15] found that the incidence of measles in cardiac children was 36 per cent, and in noncardiac children in certain public schools in New York City was 58 per cent. Among a thousand newsboys recently examined in New York City, 34 per cent reported a history of measles.[16]

Scarlet fever occurred in 42, or 10.2 per cent, of the rheumatic children, as compared with 12 per cent in the cardiac and 5 per cent in the noncardiac children in Halsey's series. Among the newsboys referred to above, 5.6 per cent reported a history of scarlet fever. Coombs[10] has referred to the significance of scarlet fever as a precursor of rheumatic heart disease. Hector[17] suggests that "the almost invariable result of scarlet fever upon the heart already damaged by rheumatism may be a rekindling of the old affection which in some cases had been quiescent for a considerable period, and that a mild or moderate attack of scarlet fever is quite capable of bringing this about." It is interesting to note, that like the various manifestations of rheumatism, and unlike measles and tonsillitis, scarlet fever occurred most often, in 38.3 per cent of the cases, between the ages of

TABLE III

INCIDENCE OF MEASLES AND SCARLET FEVER BY AGE GROUPS

AGE IN YEARS	MEASLES		SCARLET FEVER	
	NO.	PER CENT	NO.	PER CENT
Under 3	54	24.3	6	14.2
3 to 5	82	36.9	11	26.2
6 to 9	49	22.2	16	38.3
10 and over	2	0.9	6	14.2
Unknown	35	15.7	3	7.1
Total	222	100.0	42	100.0

six and nine years (Table III). Fig. 10 shows the chronological relation of scarlet fever to manifestations of rheumatic infection. In 21, or 54.3 per cent, of the cases it preceded a rheumatic manifestation; in 6, or 15.4 per cent, it occurred in the same year with the first manifestation of rheumatic infection, and in 12, or 30.7 per cent, it followed a rheumatic manifestation.

The age incidence of scarlet fever as reported in 3940 cases seen in the Willard Parker Hospital in the years 1919 to 1923, inclusive, is highest (31.8 per cent) between the ages of six and ten, and (25.4 per cent) between the ages of three and five.[18] That is to say, the age incidence of scarlet fever is similar to that of rheumatic infection. The common association of polyarthritis and chorea with scarlet fever may be due to this factor.

12. *Relative Incidence of Various Manifestations.*—An analysis of 413 case records which form the basis of this report shows the incidence of manifestations of rheumatic infection to be as follows:

A. *Polyarthritis* was the most frequent major manifestation noted, occurring from one to six times or more in each of 272 children, 65.8

per cent (Fig. 11). It was the most common manifestation found at onset, occurring in 169 children, or 40.9 per cent (Fig. 3). As a first manifestation of infection it appeared most frequently between the ages of six and nine years, in 41.4 per cent of the children. In 30.8 per cent it occurred between the ages of three and five. It occurred as a first manifestation under three years of age in only 9 children.

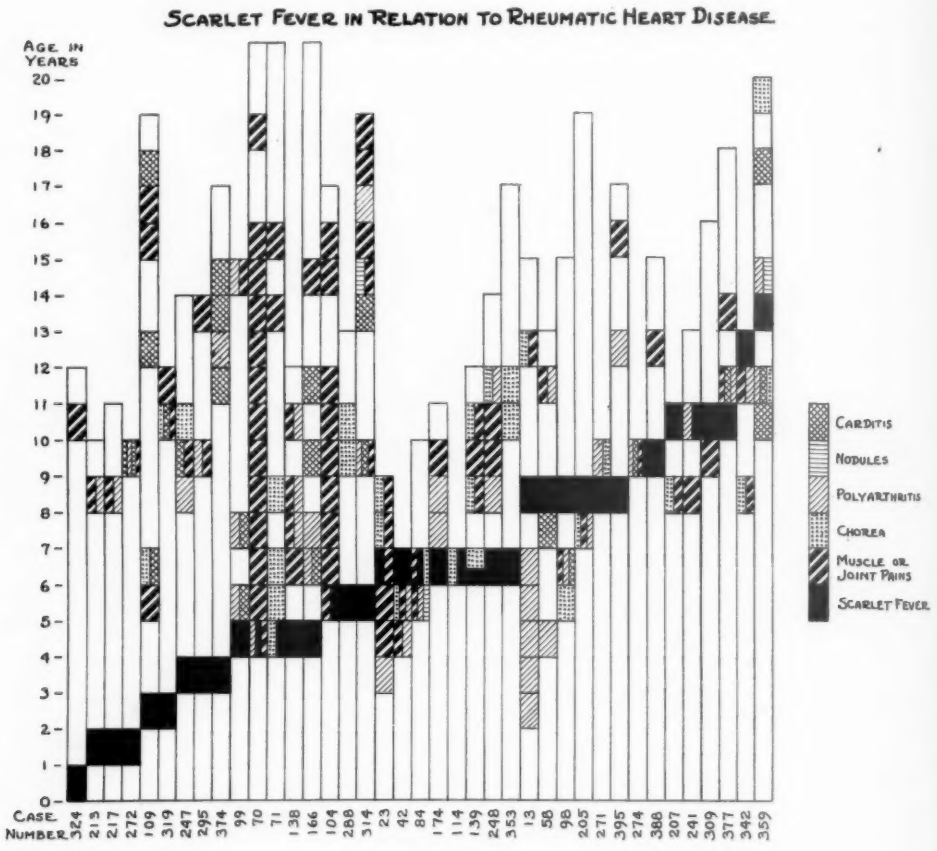


Fig. 10.

B. *Growing and Joint Pains* occurred in each of 278 children, or 67 per cent (Table IV). As the first manifestation of infection they occurred in 26.6 per cent. In more than half the children, 53.6 per cent, they occurred, like polyarthritis, as a first manifestation, between the ages of six and nine (Fig. 3). In 64 cases, or 23 per cent, they preceded the so-called major manifestations, chiefly polyarthritis. In half of these, major manifestations of infection followed within a year; in almost three-quarters within three years. In 10.9 per cent growing and joint pains were followed by acute carditis without any inter-

vening manifestation of polyarthritis or chorea (Table V). In 81 cases, or 29 per cent, they occurred after other manifestations, and in 87 cases, or 31.3 per cent, they occurred in the same year with, but were dissociated from, the major manifestation—polyarthritis, chorea, or carditis. In 46 children growing and joint pains were the only manifestations of rheumatic infection, except one or more attacks of tonsillitis in half the cases. In all but four of these 46 children there was some heart involvement. Only four had no evidence of heart disease when last seen. (Table IV.)

TABLE IV

MUSCLE AND JOINT PAINS RELATED TO OTHER RHEUMATIC MANIFESTATIONS

MUSCLE OR JOINT PAINS		TOTAL CHILDREN	
		NUMBER	PER CENT
Without other rheumatic manifestations		46	16.5
Preceding	Other rheumatic manifestations	64	23.1
Same year with		87	31.2
Following		81	29.2
Total		278	100.0

TABLE V

INTERVAL BETWEEN EARLIEST SYMPTOMS OF MUSCLE OR JOINT PAINS AND FIRST DEFINITE MANIFESTATION OF RHEUMATIC FEVER

JOINT PAINS PRECEDING RHEUMATIC MANIFESTATION	% OF TOTAL	TOTAL		INTERVAL IN YEARS					
				LESS THAN 1 YR.		1 TO 2 YR.		3 TO 5 YR.	
		NO.	%	NO.	%	NO.	%	NO.	%
Joint Pains Preceding Polyarthritis	67.2	43	100	23	53.5	11	25.6	9	20.9
Joint Pains Preceding Chorea	21.9	14	100	4	28.6	3	21.4	7	50.0
Joint Pains Preceding Carditis	10.9	7	100	5	71.4	1	14.3	1	14.3
Total	100.0	64	100	32	50.0	15	23.4	17	26.6

Growing and joint pains are usually recognized as minor manifestations of rheumatic infection. We believe, however, that their significance has been underestimated. It has been previously shown[19] that growing and joint pains are a manifestation of activity of the infection as judged by curves of the leucocyte count. We believe that the data presented concerning the age incidence, relative frequency of recurrence, and associated heart involvement should place growing and joint pains as a manifestation of equal significance with polyarthritis and chorea.

C. *Tonsillitis* occurred in one or more attacks in 199, or 48.2 per cent, of the children (Fig. 11). Two hundred and fourteen did not give a history of tonsillitis. As a first infection it occurred in 59, or 14.3 per cent, of the cases, the age distribution being from six to

nine years in 32.2 per cent; from three to five years in 30.5 per cent, and under three years in 28.8 per cent (Fig. 3).

D. *Chorea* occurred in one or more attacks in 177 children, or 42.8 per cent (Fig. 11). The sex distribution, contrary to expectation, did not show any striking predominance, occurring in 63.0 or 39.6 per cent of the boys and in 114 or 44.9 per cent of the girls (Fig. 12). In 14.8 per cent, or 25 children, chorea was the sole manifestation, but in only 5 of these was the heart apparently normal. As a manifestation of the first infection it occurred in 86 children, or 20.8 per cent, the most common age being, again, between six and nine years (55.7 per cent).

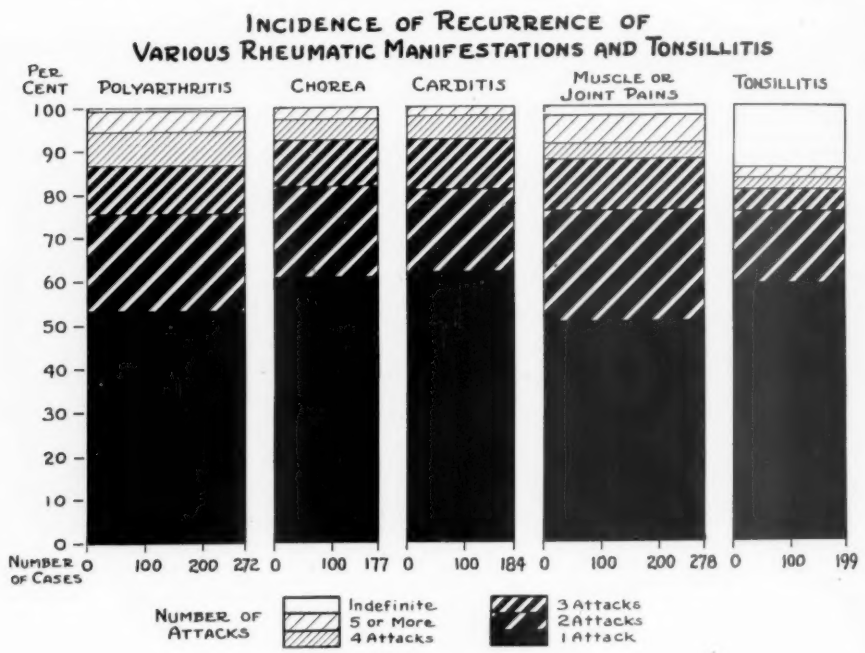


Fig. 11.

As a first manifestation of infection, chorea occurred less frequently before the age of six and more frequently after the age of ten, than any other rheumatic manifestation (Fig. 3).

E. *Nodules* were observed in 60 patients, or 14.5 per cent (Fig. 13). In 43.3 per cent of these they appeared between the ages of six and nine years, and in an equal number, after the age of nine (Fig. 14). In only eight cases did they appear under the age of five years. Twenty, or 33.3 per cent, of the children who presented nodules died, and 40, or 66.6 per cent, are living. Of those who died 60 per cent expired within one year and 80 per cent within three years after nodules were first observed. Of those still living, 45 per cent are living three or more years after nodules were first observed. Nodules occurred toward the

end of periods of active infection. They were associated, as a rule, with other severe manifestations. They appeared in three cases in which no evidence of rheumatic heart involvement has so far been observed. Twelve patients presented only mitral insufficiency, and forty-three presented severe heart involvement (Fig. 14). In a comparable series of 172 children under the age of twelve, Poynton[14] found nodules in 19 per cent. Our experience leads us to believe that nodules are not less common in the United States than in England.

F. *Rheumatic Heart Involvement.*—One hundred eighty-four children, or 44.5 per cent, either gave a history of acute rheumatic carditis or presented an attack while under observation. One hundred and fourteen of these, or 62 per cent, experienced one attack; 35, or 19.0

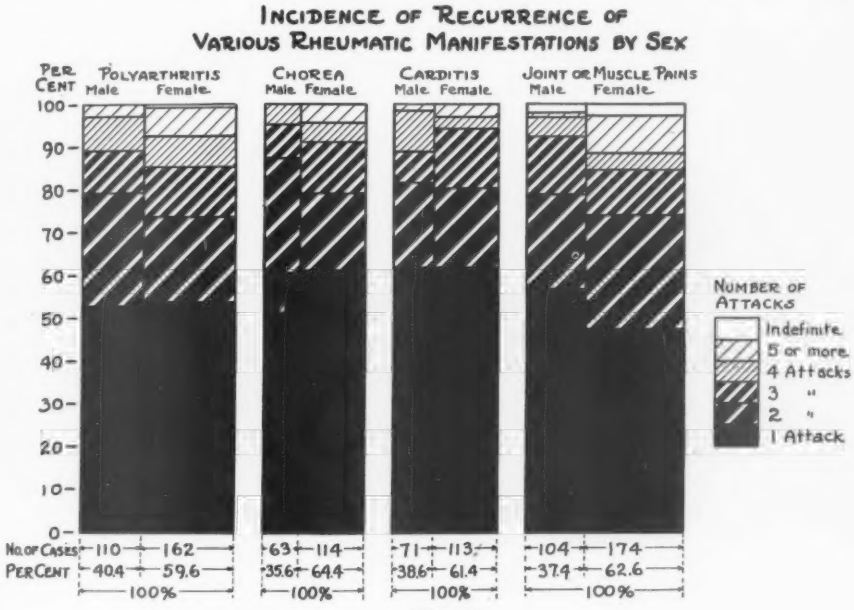


Fig. 12.

per cent, two attacks; and 35, or 19.0 per cent, three or more attacks* (Fig. 11). As a manifestation of first infection it was noted in 6.3 per cent of the cases. As a first manifestation it occurred most frequently between the ages of six and nine years, as did the other manifestations of rheumatic infection. Ten children presented at least one attack of carditis, and no other rheumatic manifestation. The symptoms of acute rheumatic carditis were frequently so slight as almost to escape detection. One hundred and twenty-eight children with rheumatic heart† disease did not give a history of any symptoms of acute

*The use of the term acute rheumatic carditis includes acute rheumatic myocarditis, endocarditis, and pericarditis.

†These observations are in accord with the common experience of discovering definite organic heart disease in older children and adults without a history of previous relative illness.

carditis (Table VII). Thirty-five developed definite heart disease while under our observation and did not present symptoms of acute carditis—the heart enlargement and the valvular lesion developing insidiously. Symptoms of congestive heart failure with edema occurred in 9 children and ended fatally in 6 cases.

Three hundred and twenty-eight, or 79.5 per cent, exhibited rheumatic heart involvement. The approximate age at onset of heart disease could be ascertained in 252 cases. In 76 the age given is doubtful.* The age at onset of the heart involvement, in the 252 cases, was between six and nine years in 45.6 per cent (Table VI).

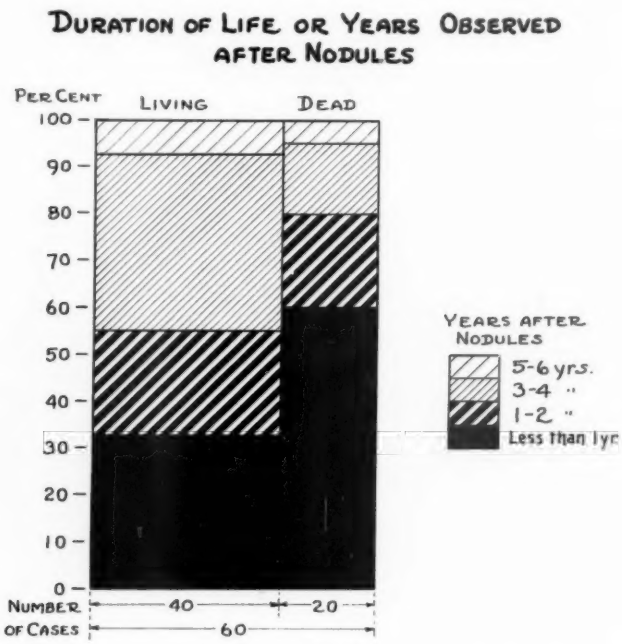


Fig. 13.

In the 76 cases in which the age at onset was doubtful, it was reported as between six and nine years in 39.5 per cent. The interval between the first manifestation of rheumatic infection and heart involvement in the 252 cases was one year or less in 63.1 per cent.† This is in marked contrast to Cohn's[1] statistics based on available published data, namely, that the interval between the beginning of infection and the establishment of chronic cardiovalvular disease ranged from one to eight years, with an average of four years.

*Where the age of onset of heart involvement was not observed but taken from the history record, the age was regarded as doubtful unless the symptoms given were characteristic.

†Mackie reports serious cardiac involvement in 68 per cent of cases, irrespective of age; an incidence of heart disease in the first attack of rheumatic fever in 61.5 per cent, of all cases under the age of five, in 78.1 per cent of cases between the ages of five and ten, and in 79.2 per cent of cases between the ages of ten and fifteen[13]

TABLE VI

INTERVAL BETWEEN ONSET OF INFECTION AND CARDIAC INVOLVEMENT RELATED TO AGE AT ONSET OF INFECTION

AGE IN YEARS AT ONSET OF INFECTION	PER CENT OF TOTAL	TOTAL		INTERVAL BETWEEN FIRST INFECTION AND CARDIAC INVOLVEMENT											
				LESS THAN 1 YEAR		1 TO 3 YEARS		3 TO 5 YEARS		6 TO 9 YEARS		10 YEARS OR MORE		UNKNOWN	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Under 3	4.0	10	100	7	70.0	0		3	30.0	0		0			
3 to 5	26.6	67	100	39	58.3	7	10.4	15	22.4	6	8.9				
6 to 9	45.6	115	100	80	69.5	19	16.5	13	11.3	3	2.6				
10 or over	14.7	37	100	33	89.2	2	5.4	2	5.4						
No record	9.1	23	100											23	100.0
Total	100.0	252	100	159	63.1	28	11.1	33	13.1	9	3.6	0		23	9.1

When related to the age at onset of infection, it appeared that the interval between initial infection and heart involvement decreased as the age at which the child became infected increased. This was not so in the case of children infected before the age of three. Since there were only 10 children in this group, it is probable, however, that the figures are too small to be significant.

13. *Potential Heart Disease.*—Of 159 children who on admission were classified as cases of "potential heart disease,"* the heart was normal

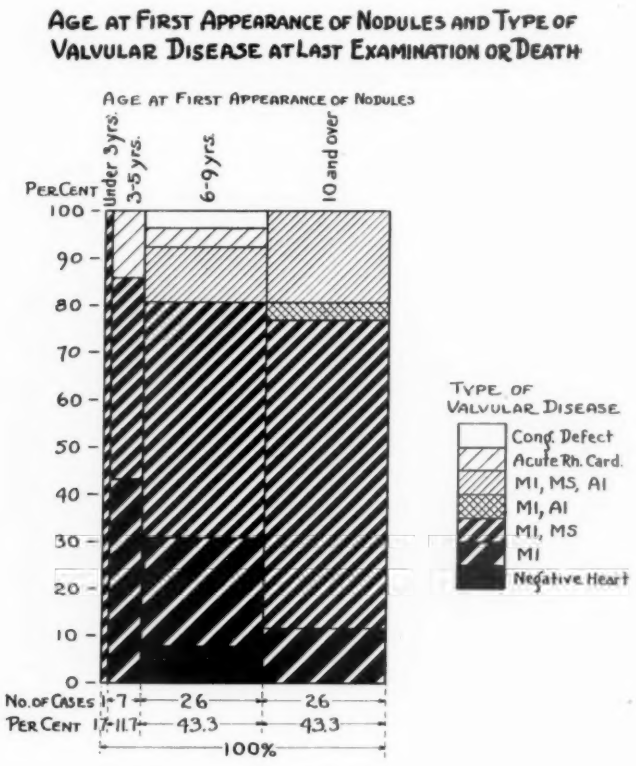


Fig. 14.

in 72, or 45.2 per cent; in 60, or 37.7 per cent, the heart was enlarged; in 11, or 6.9 per cent, a systolic murmur was present but not constant, and in 16, or 10.0 per cent, the heart was enlarged and an inconstant systolic murmur was present. Fifty-nine, or 37.1 per cent, developed definite valvular lesions; 98, or 61.6 per cent, remained in the "potential" group. Of these, 25 remained apparently normal; in 43, or 27.9 per cent, the heart became enlarged; in 6 an inconstant systolic murmur was heard, and in 24 there appeared both enlargement and an

*Potential heart disease, Class F, classification of the American Heart Association.[20] Patients without circulatory disease whom it is advisable to follow because of the presence or history of an etiological factor which might cause disease.

inconstant murmur. Five children who on admission were believed to present mitral lesions were placed in the "potential" group on final examination (Table II). If the evidence of enlargement and an evanescent murmur noted in children in the "potential" group may be considered as evidence of some rheumatic heart involvement, then the incidence of heart involvement in the 413 children with rheumatic infection would be about 91 per cent in this group. Swift[21] observed electrocardiographic evidence of some degree of functional cardiac dis-

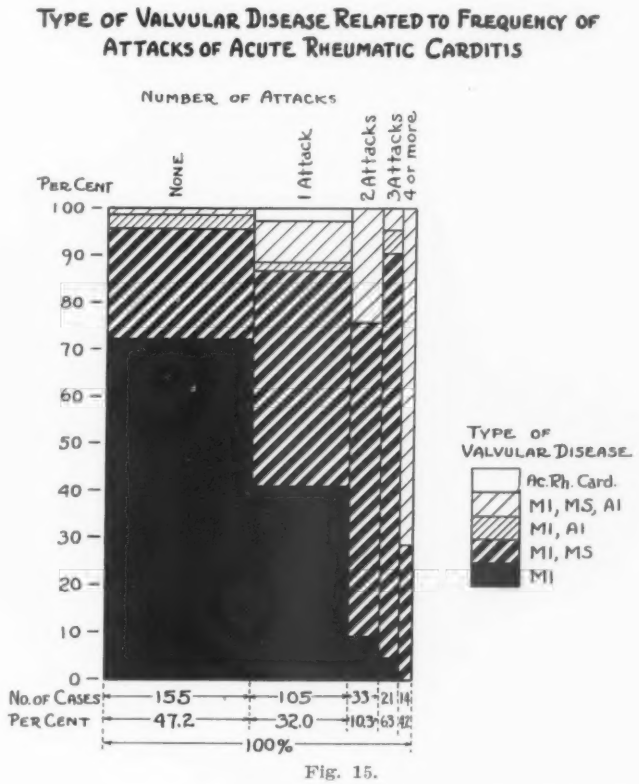


Fig. 15.

turbance in over 90 per cent of a series of 81 patients suffering from rheumatic fever. What the actual incidence of rheumatic heart involvement is, in any series of observations, depends naturally on the method of examination and the criteria used. Slight but insignificant changes in physical signs may be overlooked unless children are under constant and careful observation.

14. *Cardiac Valvular Disease.*—Three hundred and twenty-eight children presented clinical evidence of valvular heart disease. Of these, a diagnosis of mitral insufficiency was made in 48.5 per cent, mitral stenosis and insufficiency in 39.6 per cent, and aortic and mitral

disease* in 10.9 per cent. (Fig. 15.) Of 157 children who were believed to present mitral insufficiency on admission, 48 developed mitral stenosis—14 within three years, and 34 after three or more years. One developed aortic insufficiency, and 2 developed both mitral stenosis and aortic insufficiency; in 2 the heart remained enlarged, but the murmur disappeared; in 2, both the enlargement and murmur disappeared, and in one only a systolic murmur without enlargement was present when last seen. On final observation 101 remained with signs of mitral insufficiency (Table II).

The incidence of single or multiple valvular lesions seemed to be related to the number of attacks of carditis.

15. *Multiple Valvular Lesions Related to Attacks of Carditis.*—The incidence of multiple valvular lesions was greatest in children who experienced four attacks of carditis. In children who experienced two or three attacks of carditis, mitral stenosis with insufficiency was the most common lesion. The incidence of single lesions (mitral insufficiency) was most frequent in children having but one or no recognized attack of carditis (Fig. 15). A single attack was followed by mitral insufficiency in a very large number of individuals (41 per cent). This observation tends to confirm the view that cardiac involvement is a very frequent concomitant of rheumatic fever.

A comparison of the incidence of mitral stenosis in 125 children with a history of chorea, and in 176 children with a rheumatic history exclusive of chorea, showed practically no difference. If anything, mitral stenosis occurred more often in the group that had not had chorea.

16. *Heart Enlargement.*—On final observation 150 children, or 49.8 per cent of the children who were afflicted with rheumatic heart disease, showed slight heart (1+) enlargement. Ninety-two, or 30.6 per cent, showed moderate heart enlargement (2+), and 53, or 17.6 per cent, showed marked enlargement† (3+, 4+, etc.). (See Table VII.) A comparison of the size of the heart with the age of the child at the time of first and last observation shows a slight increase in size at the later date. A similar comparison of the size of the heart of children suffering from congenital heart disease, heart disease of unknown etiology, or "possible" heart disease, on first and last observation, showed no appreciable difference (Fig. 16). These observations seem to indicate that changes in the size of the heart are not related to age. A comparison of the size of the heart with the number of attacks of carditis shows an increased incidence of three-plus enlargements in

*The diagnostic criteria of the Heart Committee, New York Tuberculosis and Health Association were adhered to.[20]

†The size of the heart was arbitrarily graded one to four plus, the diagnosis being made by routine serial fluoroscopic tracings checked in questionable cases by teleoroentgenograms.

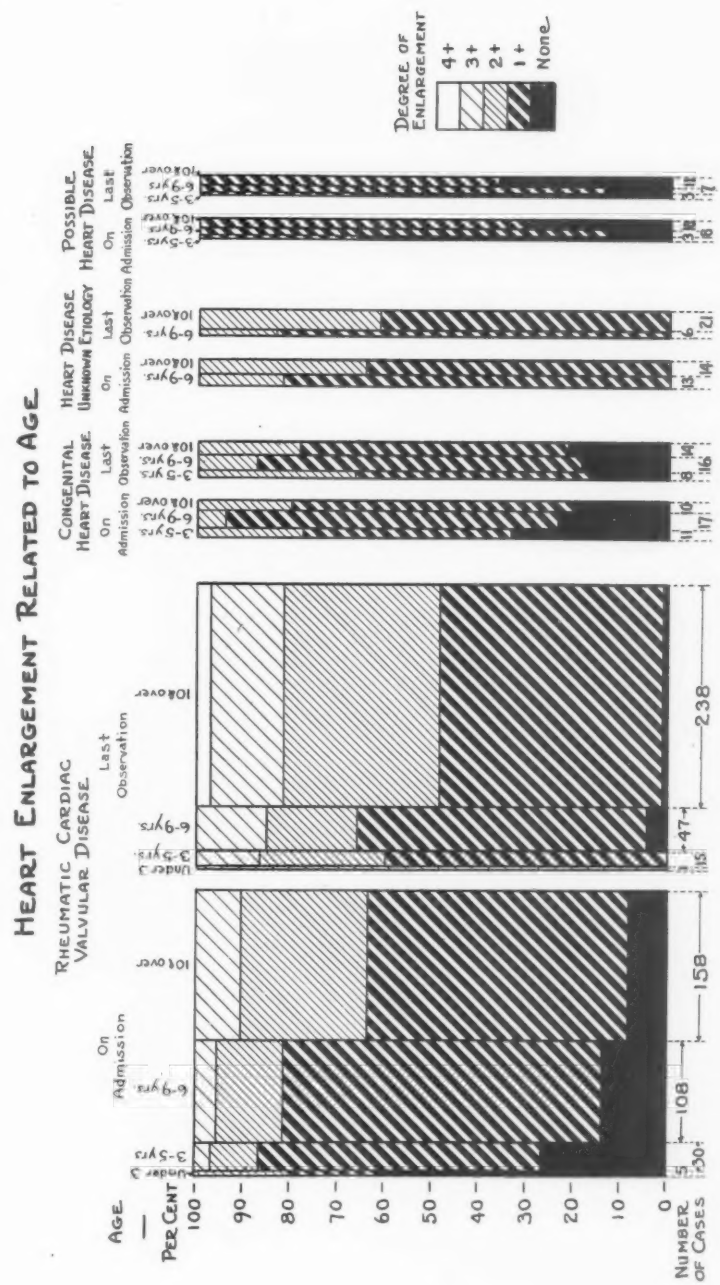

HEART ENLARGEMENT RELATED TO AGE
RHEUMATIC CARDIAC VALVULAR DISEASE
CONGENITAL HEART DISEASE
HEART DISEASE UNKNOWN ETIOLOGY
POSSIBLE HEART DISEASE
On Admission
Last Observation
AGE
PER CENT
NUMBER OF CASES
Under 3
3-5 yrs.
6-9 yrs.
10 & over
DEGREE OF ENLARGEMENT
4+
3+
2+
1+
None
100
90
80
70
60
50
40
30
20
10
0
5
30
108
158
115
47
238
11
17
9
16
13
14
6
21
3
18
3
18
3
17

Fig. 16.

TABLE VII

HEART ENLARGEMENT IN RELATION TO NUMBER OF ATTACKS OF CARDITIS IN 301 CASES OF RHEUMATIC HEART DISEASE

CARDITIS	% OF TOTAL	TOTAL		DEGREE OF ENLARGEMENT											
				1+		2+		3+		4+		NONE		UNDETERMINED	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
1 attack	34.8	105	100	43	40.9	40	38.1	17	16.2	1	1.0	1	1.0	3	2.8
2 attacks	11.0	33	100	6	18.2	12	36.4	11	33.3	4	12.1	0		0	
3 attacks	6.9	21	100	4	19.0	8	38.1	8	38.1	1	4.8	0		0	
4 or more attacks	4.6	14	100	1	7.1	3	21.4	9	64.3	1	7.1	0		0	
None	42.7	128	100	96	75.0	29	22.8	1	0.8	0		2	1.4	0	
Total	100.0	301	100	150	49.8	92	30.6	46	15.3	7	2.3	3	1.0	3	1.0

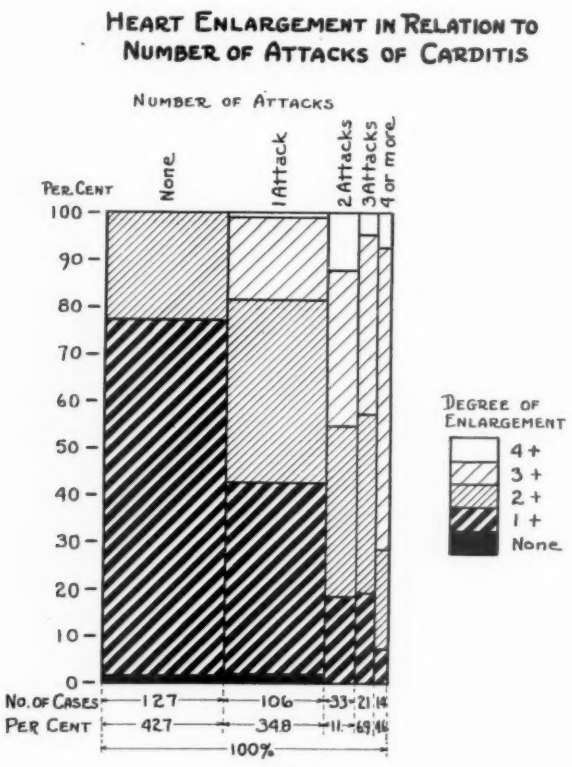


Fig. 17.

children who experienced four or more attacks of carditis (Fig. 17). In our experience, then, the degree of heart involvement, as determined clinically by the size of the heart and the number of valves involved seems closely related to the number of recurrent attacks of acute rheumatic carditis, rather than to the age of the child.

17. *Functional Classification.*—On final observation 313 children with rheumatic heart disease were classified according to functional capac-

ity. Seventy and six-tenths per cent were found to be in Class I; 11.2 per cent in Class IIA; 1.9 per cent in Class IIB, and 13.1 per cent in Class III.[20] These figures indicate that the majority of children with rheumatic heart disease are able to tolerate a normal amount of work and exercise.

18. *Rate and Rhythm.*—Pathological arrhythmias are infrequent in children. In this series 8 children developed auricular fibrillation. All of these cases were fatal. One child with congenital heart disease suffered from repeated attacks of paroxysmal tachycardia.

COMMENT

If it may be assumed that these 500 children observed over a period of ten years comprise a representative sample of children attending a heart clinic in New York City the resulting statistics, although based on a small number, may be taken as indicating the status of heart disease in children of the class and age groups that were studied. Accumulation of such statistics collected in a uniform manner will correct such inaccuracies as may be due to smallness of number or lack of the representativeness of the sample.

From these data it is apparent that rheumatic infection is the most common etiological factor in the causation of heart disease in childhood. The clinical course is in marked contrast to that which obtained in children with nonrheumatic heart involvement. The latter retained the same physical signs, without progression, over a period of years.

A consideration of the data presented on the natural history of rheumatic infection in its relation to heart disease suggests that rheumatic infection as observed in children is a general infection. It attacks mainly children of school age, six to nine years; its course is characterized by frequent periods of activity, these being most frequent during the first three years after onset, and followed by a diminishing number of recurrences. The diminution is particularly noticeable after the age of twelve when what may be called immunity seems to be developing. The ages under three and from ten to fourteen appear to be critical periods of particular vulnerability, as judged by the rate of mortality and by the increased activity of the disease at these age periods.

In this study periods of activity of infection included symptoms of growing and joint pains, polyarthritis, chorea, nodules and acute carditis. Other recognized associated symptoms were not utilized for statistical analysis because it was not believed that such data could be obtained with sufficient accuracy from a history record. Since these manifestations were always associated with the aforementioned symptoms, the exclusion of the former did not appreciably influence the final statistical correlations.

The heart is probably always affected at the onset of this disease, Although, as has been indicated, its involvement is not always detected clinically. In 63 per cent of the cases the interval between the onset of infection and definite heart involvement was one year or less. The extent of the involvement of the heart increased with repeated periods of activity, and seemed to remain the same in quiescent periods. The type of associated manifestation did not seem to be related to the onset or degree of heart damage.

It seems, then, that in children rheumatic infection manifests itself as a general infection in which the heart is probably the first and main seat of involvement, although this fact is often obscured because the associated manifestations appear more prominent, being, as they are, more easily recognized clinically.

Comparison between various statistical studies of rheumatic infection is difficult. Studies which include adults are not always comparable with observations limited to children, nor are those which view rheumatic polyarthritis and chorea as separate clinical entities, with heart disease as a complication, comparable with our conception of rheumatic infection. If the conception which we adopt is valid *the prevention of heart disease in children means the prevention of rheumatic infection.*

In judging the results of therapeutic measures of prevention or control it is necessary to have in mind the influence of age on the course of the disease; that is to say, the influence of age on increasing susceptibility, up to a certain period, and developing immunity.

SUMMARY

1. Of 500 children ranging in age from two to twenty-two years, observed in a heart clinic, four-fifths presented a rheumatic history.

2. Congenital heart defects occurred in 50, or 11.2 per cent. In 18 of these there was subsequent rheumatic infection.

3. Children with "possible heart disease" (systolic murmur heard between the second and fourth left interspaces) retained the same physical signs without progress over a period of years.

4. The average age at onset of rheumatic infection was 7.3 years. In one-half the children the onset occurred between the ages of six and nine years.

5. Rheumatic infection concerns itself primarily with children of the grade-school age; about the age of twelve the tendency to infection begins to diminish.

6. Three-fourths of 413 children with a rheumatic history developed definite heart disease and one-fourth were "potential heart disease" cases.

7. The heart is probably always involved to some extent at the time of the first infection (some evidence of involvement was noted in 91 per cent at the time of last observation), although marked involvement was noted in only 63 per cent within one year of onset.

8. The associated manifestations of rheumatic infection were not indicative of the degree of heart involvement. Growing and joint pains bear the same relation to heart involvement as polyarthritis or chorea.

9. The degree of heart involvement seemed closely related to the number of attacks of carditis.

10. Twelve per cent of the children died. Eighty-eight per cent of the deaths were due to rheumatic heart disease. The most common age at death was between eleven and fourteen years.

11. The earlier the age of onset of infection the greater is the number of recurrences. The later the age at onset the greater is the number of recurrences within one year.

CONCLUSION

Accumulation of statistical data collected in a uniform manner will lead to a better understanding of heart disease in children, particularly rheumatic heart disease.

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STATISTICAL STUDIES BEARING ON PROBLEMS IN THE CLASSIFICATION OF HEART DISEASE

IV. Tonsillectomy in Its Relation to the Prevention of Rheumatic Heart Disease*

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INTRODUCTION

TONSILLECTOMY is an old surgical procedure. Glover[1] states that the tonsils were removed as early as 10 A.D. Today tonsillectomy has become so commonplace that it is almost a routine in childhood.

The function of the tonsil has not been definitely ascertained. Digby[2] believes that the tonsil plays an important function in immunizing the body against pathogenic bacteria. Canfield[3] believes that a child is more susceptible to infection following tonsillectomy and adenoidectomy. This observation is in accord with the clinical experience of many.

Opinions differ concerning signs that are indicative of disease of the tonsils. Coakley‡ suggests that attention be paid to:

1. The distribution of lymphoid tissue of the lingual tonsils, the nasopharynx, nasal mucosa, the posterior pharyngeal wall, the lateral aspect of the pharynx behind the posterior pillars and below the tonsil on the lateral aspect of the pharyngeal wall, and infection of the para-nasal sinuses and mastoid.
2. The so-called "embedded" tonsil.
3. The thin, creamy secretion that comes from the upper portion of the tonsils.
4. The history of repeated attacks of tonsillitis.
5. Injection of the plica and the anterior pillars of the fauces.

The frequent occurrence of tonsillitis or sore throat in children subject to rheumatic infections has suggested that the tonsil is the probable portal of entry and focus of infection. Tonsillitis and sore throat are, however, common complaints and, certainly, in the majority of cases these affections are not followed by the rheumatic cycle. Maclachan[4] believes that the tonsils are probably more fre-

*Paper No. 2, from the Department of Pediatrics, Cornell University Medical College, the Heart Clinic of the New York Nursery and Child's Hospital and the Research Committee of the Heart Committee of the New York Tuberculosis and Health Association.

Read before the Committee on Cardiac Clinics, New York, N. Y., October 20, 1928.

†Working on behalf of the Research Committee of the Heart Committee of the New York Tuberculosis and Health Association.

‡Personal communication forming a memorandum for use by the Committee on Cardiac Clinics of the Heart Committee of the New York Tuberculosis and Health Association.

quently subject to acute inflammation than any other organ of the body, and that those who escape one or more attacks of sore throat may be regarded as exceptions. He concludes from an extensive pathological study that the disease is pyogenic rather than rheumatic in origin, the ulcers at the base of the crypts being the portal of entry of organisms. Similarly, Groedel[5] believes that this affection is a local condition permitting the entrance of certain streptococci and that rheumatism follows only where there is a predisposition to the disease.

That tonsils are not the only possible portal of entry for infection from the mouth is evident when one considers the lymphoid structures constituting Waldeyer's tonsillar ring. Complete tonsillectomy and adenoidectomy cannot remove all this lymphoid tissue. Following operation there is, furthermore, frequently hyperplasia of numerous lymphoid follicles in the nasopharynx and tonsillar fossa. Tonsillectomy is, nevertheless, a therapeutic measure which is widely recommended for the prevention of rheumatic infection in children.

REVIEW OF THE LITERATURE

A review of the literature on the value of tonsillectomy in the prevention of the occurrence and recurrence of manifestations of the rheumatic syndrome is inconclusive. As Cohn[6] has pointed out, the period of observation has frequently been too short and the cases have not been reported in sufficient detail to follow the course of the disease in each individual.

A brief review of the literature may best be undertaken, perhaps, by reproducing Cohn's[6] table, with the addition of experiences reported since its publication (Table I). The number of treated cases reported on in sufficient detail to be included in this table is 1,232. Of these, recurrences of manifestations of rheumatic infection were noted in 43.1 per cent, and no recurrences in 56.7 per cent. Opinions differ among the observers concerning the results of the operation on the recurrence of rheumatic fever.

Period of Observation.—In few instances only did the average length of time of observation after the operation exceed three or four years. A summary of cases reported in the literature about which adequate details were published to make possible tabulation indicates that recurrences became more frequent as the period of observation was extended (Table II).

Age at Operation.—It is to be noted that the age at which the enucleation of tonsils was performed was not considered by any of the observers whose reports are reviewed in Table I. In only 222 instances was the age at operation together with the ages at which subsequent manifestations of infection appeared given in the publications. Tabulation of these data reveals that as the age at which the tonsils

TABLE I[6]

TONSILLECTOMY: ITS EFFECT ON THE OCCURRENCE OF RHEUMATIC MANIFESTATIONS

DATE	AUTHOR	NO. CASES TOTAL	WITH TONSILLECTOMY NO.	WITH TONSILLECTOMY PER CENT	NO RECURRENCE NO.	NO RECURRENCE PER CENT	WITH RECURRENCE NO.	WITH RECURRENCE PER CENT	WITHOUT TONSILLECTOMY NO.	WITHOUT TONSILLECTOMY PER CENT	NO DEVELOPMENT OF MANIFESTATIONS NO.	NO DEVELOPMENT OF MANIFESTATIONS PER CENT	WITH DEVELOPMENT OF MANIFESTATIONS NO.	WITH DEVELOPMENT OF MANIFESTATIONS PER CENT	REMARKS
Complete Tonsillectomy															
1908	Rosenheim		10		10	100.0	0	0							
1911	Archibald	7	7		5	71.4	2	26.8							
1915	Young	21	21		6	28.6	15	71.4							
1917	Crowe, Watkins and Rothholz	49	49		28	56.3	21	43.7							
1920	St. Lawrence	85	85		54	63.5	31	36.5							
1923	Hunt and Osman	144	66		31	47.0	35	53.0	78		45	58.0	33	42.0	All cases
		(99)	(50)				(23)	(46)	(46)				(15)	(33)	After first attack
		(48)	(16)				(12)	(75)	(32)				(18)	(56)	After later attacks
1924	Ingerman and Wilson	167	70		17	24.0	53	76.0	97		19	19.6	78	80.4	
1924	Dulaney		22		22	100.0	0	0							
1926	R. Miller	133	45		18	40.0	27	60.0	(83)						
1926	R. Miller (A. P. Thompson)	16	6		6		10	62.5							
1926	Mackie	299	80		46	57.5	34	42.5	207		82	39.7	125	60.3	After first attack
			12		0	0									Before first attack
1927	Robey and Freedman[7]	454	169		122	72.1	47	27.9	212		160	75.5	52	24.5	
1927	Kaiser[8]	525	525		316	60.0	209*	39.8							Rheumatism
		102	65		18	27.7	47†	72.1							Chorea
Totals			1232		699	56.7	531	43.1	594		396	51.5	288	48.5	Rheumatism
Partial Tonsillectomy															
1921	St. Lawrence	9	9		1	11.2	8	88.8							
1924	Ingerman and Wilson	18	18		4	22.3	14	77.7							
1927	Robey and Freedman	32	32		17	53.2	15	46.8							
Totals		59	59		22	37.3	37	62.7							

*93 occurred for the first time after operation.
†32 occurred for the first time after operation.

TABLE II*

TONSILLECTOMY

RECURRENCE OF RHEUMATIC FEVER AND CHOREA AND THE DURATION OF OBSERVATION

MANIFESTATION	DURATION OF OBSERVATION AFTER TONSILLECTOMY YEARS	CASES EXHIBITING MANIFESTATIONS BEFORE TONSILLECTOMY		AFTER TONSILLECTOMY					
				RECURRENCE				NO RECURRENCE	
				SAME MANIFESTATION		OTHER MANIFESTATION			
		NO.	%	NO.	%	NO.	%	NO.	%
Rheumatic fever	1 or less	16	100	2	12.5	3	18.7	11	68.7
	1 to 3	61	100	9	14.7	17	27.9	35	57.4
	More than 3	41	100	16	24.4	10	24.4	21	51.2
	No report	5	—	2	—	0	—	3	—
Chorea	1 or less	7	100	1	14.3	2	28.6	4	57.1
	1 to 3	51	100	17	33.3	8	15.7	26	51.0
	More than 3	26	100	12	46.2	1	3.8	13	50.0
	No report	9	—	8	—	0	—	1	—

*Table compiled from reports of Young,[9] Crowe, Watkins and Rothholz,[10] St. Lawrence,[11] and Ingerman and Wilson.[12]

TABLE III*

TONSILLECTOMY
RELATION OF SUBSEQUENT MANIFESTATION TO AGE

AGE AT OPERATION YEARS	TOTAL		RECURRENCE		NO RECURRENCE	
	NO.	%	NO.	%	NO.	%
0-5	28	100	17	61.	11	39.
6-9	88	100	49	56.	39	44.
10 and over	106	100	53	50.	53	50.
TOTAL	222	100	119	54.	103	46.

*Table includes data reported by Crowe, Watkins and Rothholz,[10] St. Lawrence,[11] and Ingerman and Wilson.[12]

were enucleated increased, the proportion of cases that recurred to those that did not recur decreased (Table III).

Controls.—In only four* of the series reported were corresponding untreated groups studied as controls, and in only two† did the treated children show a lesser incidence of recurrence than the untreated. Even in these two series, however, as many as 80.4 per cent and 60.3 per cent of the untreated children suffered at least one return of the rheumatic condition. It is to be regretted that Kaiser,[8] although he gives the incidence rate of the various rheumatic manifestations upon the treated and untreated children, does not specify whether the incidence of infection among the latter occurred during a period comparable in duration with that which elapsed in the treated cases after the time of operation. As was pointed out in an editorial in a recent issue of *The Lancet*, there is no justification for his statement that "It is fair to conclude that the tonsils undoubtedly are a focus in many cases of rheumatic fever. Their removal offers considerable protection against recurrent attacks, and when the tonsils are removed before symptoms have developed, the chances for escaping rheumatic infection are appreciably increased."

Obviously, when opinions cover so wide a range as those which we have repeated, knowledge concerning this matter is still imperfect. The literature of this subject is large, but contains, we think after reviewing it, few descriptions of the disease or of cases that lend themselves to critical analysis. It has seemed to us to be more important to report the results of our studies than to review data which are either incomplete or are collected from points of view which are preconceived.

INFLUENCE OF TONSILLECTOMY ON THE COURSE OF THE RHEUMATIC INFECTION IN CHILDREN

In this investigation we have made use of the records of 413 rheumatic children reported in a previous paper.[15] These children were observed over a period ranging from one to ten years. In 247 cases

*Hunt and Osman,[6] Ingerman and Wilson,[12] Mackie,[14] Robey and Freedman.[7]
†Ingerman and Wilson[12] and Mackie.[14]

the tonsils were removed. The remaining 166 served as controls. We have attempted to present the data in detail* and to analyze the results, bearing in mind the age of the child at the time of operation, the age at the onset of the infection, and the period of observation after operation. There are included as recurrences of manifestations of infection (evidence of activity) polyarthritis, growing and joint pains, chorea, nodules, and carditis. Tonsillitis was not included, for reasons stated in a previous paper[15] and therefore will be considered separately.

Recurrence of Infection After Tonsillectomy.—Of 245† children subjected to tonsillectomy, manifestations of rheumatic infection recurred in 117, or 47.7 per cent; infection appeared for the first time in 85, or 34.7 per cent; that is to say, there was a total incidence of rheumatic infection subsequent to tonsillectomy in 202 cases, or 82.4 per cent of all children operated upon. In only 43 cases, or 17.5 per cent, therefore, was there no manifestation of rheumatism after the operation (Table IV).

TABLE IV

TONSILLECTOMY

RELATION OF SUBSEQUENT MANIFESTATION TO AGE

AGE AT OPERATION YEARS	% OF TOTAL	TOTAL		AFTER TONSILLECTOMY					
				RECURRENCES		FIRST INFECTION		NO RECURRENCE	
		NO.	%	NO.	%	NO.	%	NO.	%
0-5	22.8	56	100	17	30.4	35	62.5	4	7.1
6-9	47.4	116	100	59	50.9	41	35.3	16	13.8
10 and over	29.8	73	100	41	56.2	9	12.2	23	31.5
Total	100.0	245	100	117	47.7	85	34.7	43	17.5

TABLE V

TONSILLECTOMY

RELATION OF SUBSEQUENT MANIFESTATION TO AGE

AGE AT OPERATION YEARS	TOTAL		AFTER TONSILLECTOMY					
			RECURRENCES		FIRST INFECTION		NO RECURRENCE	
	NO.	%	NO.	%	NO.	%	NO.	%
0-5	56	22.8	17	14.5	35	41.1	4	9.3
6-9	116	47.4	59	50.5	41	48.3	16	37.2
10 and over	73	29.8	41	35.0	9	10.6	23	53.5
Total	245	100.0	117	100.0	85	100.0	43	100.0

Age at Operation and Recurrent Infection.—In 116 patients, or 47.4 per cent, almost one-half, the operation was performed at ages between six and nine years (Table IV). It is important to note that this is also the age at which the greatest number of children became in-

*The age at tonsillectomy, age at onset of infection, and at recurrences of various manifestations of infection have been charted for each child in Fig. 6 in a previous paper.[15]

†Two cases were omitted in the tabulations because of incomplete data.

fected. It is important to note, also, that of children infected after operation, tonsillectomy was performed between the ages of six and nine in approximately 50 per cent of the cases. (Table V.) Of the treated children who did not experience subsequent infection, however, the operation was performed in half of the cases after the age of ten years was reached. As was indicated in the previous paper, there appears to be a diminution in susceptibility to rheumatic infection beginning at about the age of ten. It seems probable, therefore, that the age at which the operation was performed, and not the operation itself may be the significant factor in the incidence of nonrecurrence.

This point is further emphasized when we consider the relative incidence of recurrence and nonrecurrence in groups of children oper-

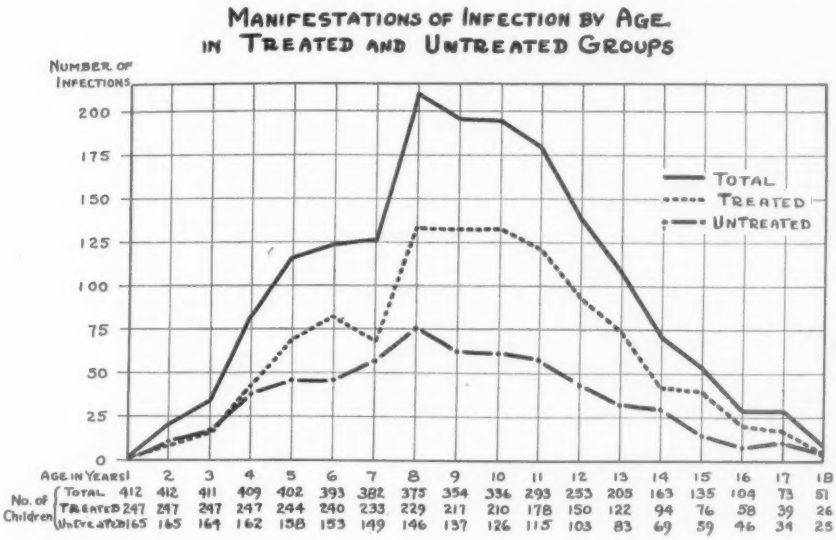

Fig. 1.

ated on at different ages. When the age is less than five years, 7.1 per cent experienced no recurrence; of those operated upon between the ages of six and nine, 13.8 per cent did not recur, and at age ten or over, 31.5 per cent were not followed by recurrences (Table IV). In other words, as the age at operation increases, the likelihood of recurrence diminishes.

Incidence of Recurrent Infection in Treated and Untreated Groups.—As was previously pointed out, beginning at two years, the incidence of manifestations of infection increases with each succeeding age, reaches a peak at the age of eight, and then gradually but progressively declines. This was found to be true in both treated and untreated children. In general, the trend of the curves is the same for both groups (Fig. 1).

From our experience in the observation of 245 treated and 165* untreated children, we have attempted to learn what the likelihood is of recurrence at each age for children in both groups (Fig. 2). The ordinates (Curves A and B) show the average number of manifestations of infection which a child has experienced before a given age. In Curve A, this is the number before operation. In similar fashion Curves C and D show the average number of infections experienced after each age. In the case of Curve C it is the average number of infections experienced after operation. The curves lead us to expect, for instance, that a child that presents itself for operation at the age of six years will have suffered, on the average, one attack of infection, but that after operation it will yet experience more than three, probably four, attacks. A child of like age not operated upon, while

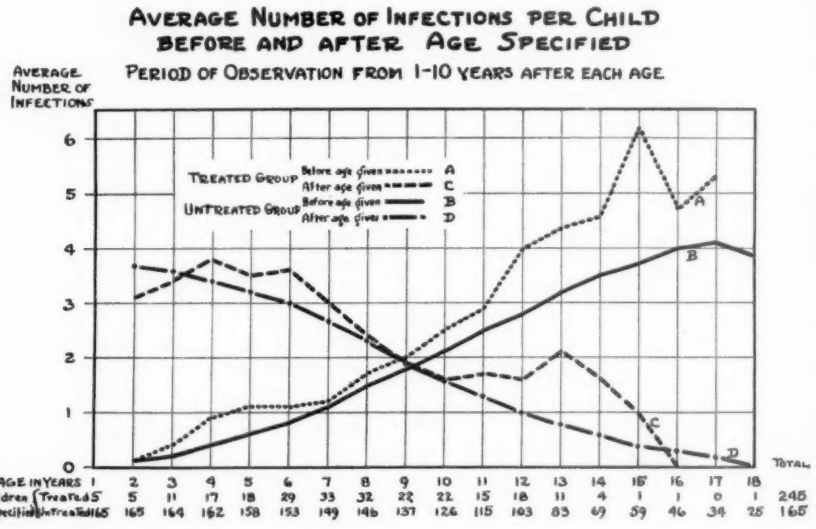
AVERAGE NUMBER OF INFECTIONS PER CHILD BEFORE AND AFTER AGE SPECIFIED
PERIOD OF OBSERVATION FROM 1-10 YEARS AFTER EACH AGE
AVERAGE NUMBER OF INFECTIONS
TREATED GROUP
Before age given A
After age given C
UNTREATED GROUP
Before age given B
After age given D
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 TOTAL
No. Children Treated 5 11 17 18 29 33 32 22 22 15 18 11 4 1 1 0 1 245
at age specified Untreated 165 165 164 162 158 153 149 146 137 126 115 103 85 69 59 46 34 25 165

Fig. 2.

it will have experienced a somewhat lesser number of infections, will likewise experience about three times as many attacks in subsequent years. Similarly, a child that presents itself for operation at the age of thirteen years will have suffered, on the average, four attacks and is likely to exhibit after operation two more attacks. A child of like age not operated upon is likely to experience but one subsequent attack.

In general, these curves seem to express the following:

1. As the age increases, the average number of attacks of infection a child may anticipate decreases. At nine years, the average child will have suffered (Curves A and B) as many attacks as it will experience in subsequent years (Curves C and D).

*One case was omitted in the tabulation because of incomplete data.

2. This is true whether a child has or has not been operated upon. The curves for the two groups are almost parallel. In both groups the incidence of infection increases with age (Curves A and B).

3. Although the curves for the two groups are approximately parallel, those representing the untreated children are at almost every point lower than those representing the treated group. That is to say, at each age the untreated children experienced fewer infections than did those that were treated. One may assume from these figures that the untreated children were less susceptible to recurrent attacks of infection and that, perhaps, for this reason they were not subjected to tonsillectomy—a therapeutic measure often applied, especially to cases of severe and recurrent infection, in the absence of knowledge of more certain therapy. On the basis of this assumption, the untreated children in this series do not constitute a perfect control group.

4. Excision of the tonsils seems to have no effect on the recurrence of rheumatic infection.

If this analysis of our data is correct, it may be an explanation of the contradictory results obtained by various observers concerning the effect of tonsillectomy in rheumatic children. If the majority of the children reported on in any series have reached an age of ten years or more at the time of operation, the results of the operation might appear to be favorable as judged by recurrent infection. If, on the other hand, the sample is overloaded with cases that were operated on at earlier ages, a high incidence of recurrence would be the probable result and the benefit of tonsillectomy would very likely be questioned.

Period of Observation.—A study of the literature reveals the fact that the percentage of recurrences in treated children increases with time (Table II). We have attempted to consider this factor by drawing curves similar to those already presented, limiting our data in each case to children who were observed for varying numbers of years after each age (Fig. 3). In general, the curves are in agreement with our first series. At every age subsequent to an age ranging from seven to nine years, a child, on the average, experienced fewer attacks of infection than it had before the age specified.

It is apparent from these curves, also, that the longer the period of observation, the greater is the average number of infections at each susceptible age. This is true in the treated as well as in the untreated groups. After the age of nine years, when, as we have shown, susceptibility to infection appears to be lessened, prolonged periods of observation have no effect on the number of recurrences.

Tonsillitis.—Of the 247 children from whom the tonsils were removed, 124, or 50.2 per cent, experienced recurrent tonsillitis, and 123, or

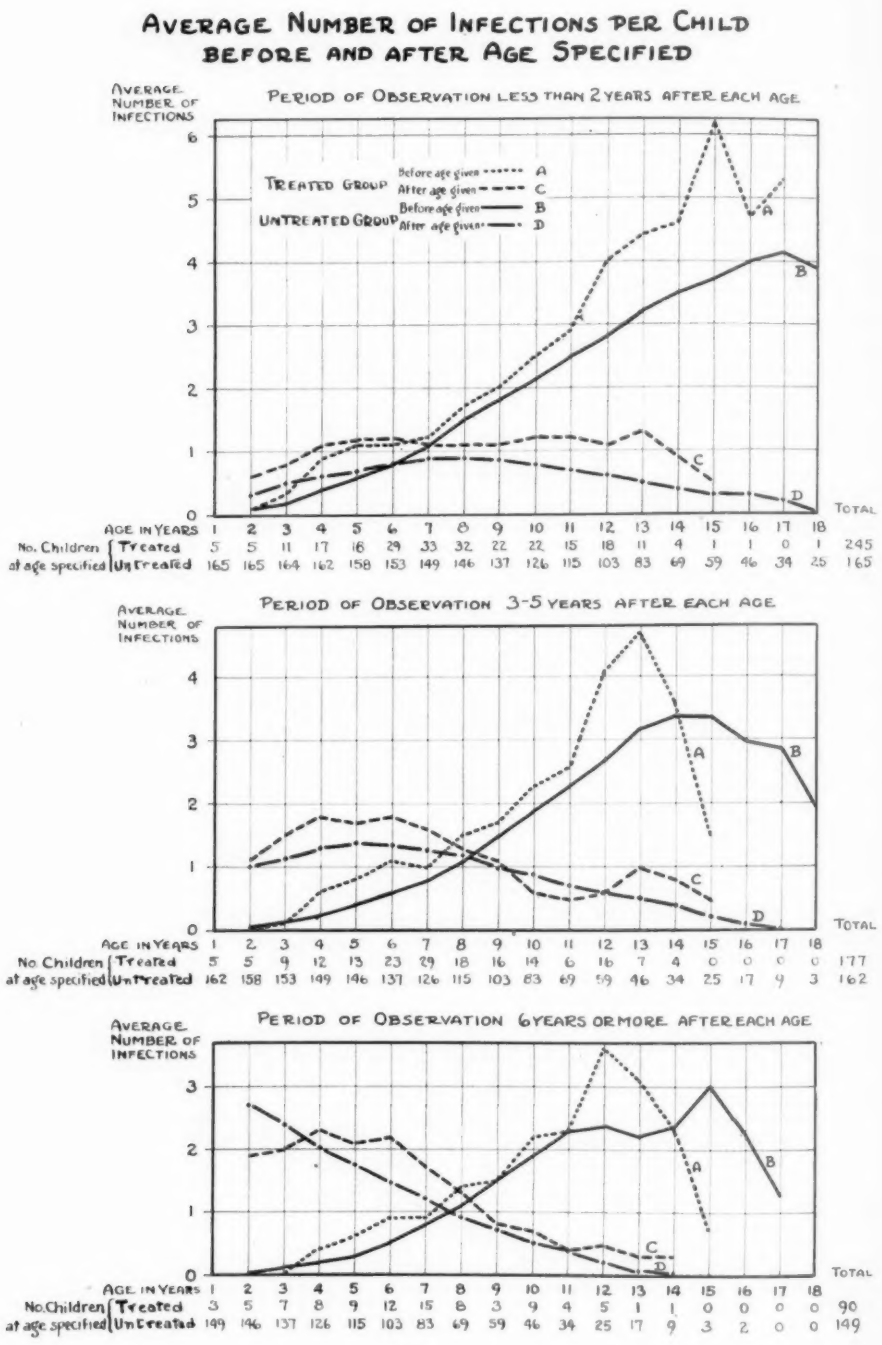
AVERAGE NUMBER OF INFECTIONS PER CHILD BEFORE AND AFTER AGE SPECIFIED
AVERAGE NUMBER OF INFECTIONS
PERIOD OF OBSERVATION LESS THAN 2 YEARS AFTER EACH AGE
TREATED GROUP
Before age given A
After age given C
UNTREATED GROUP
Before age given B
After age given D
TOTAL
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
No. Children at age specified Treated 5 5 11 17 16 29 33 32 22 22 15 18 11 4 1 1 0 1 245
Untreated 165 165 164 162 158 153 149 146 137 126 115 103 83 69 59 46 34 25 165
PERIOD OF OBSERVATION 3-5 YEARS AFTER EACH AGE
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
No. Children at age specified Treated 5 5 9 12 13 23 29 18 16 14 6 16 7 4 0 0 0 0 177
Untreated 162 158 153 149 146 137 126 115 103 83 69 59 46 34 25 17 9 3 162
PERIOD OF OBSERVATION 6 YEARS OR MORE AFTER EACH AGE
AGE IN YEARS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
No. Children at age specified Treated 3 5 7 8 9 12 15 8 3 9 4 5 1 1 0 0 0 0 90
Untreated 149 146 137 126 115 103 83 69 59 46 34 25 17 9 3 2 0 0 149

Fig. 3.

TABLE VI

TONSILLECTOMY

INCIDENCE OF TONSILLITIS IN TREATED AND UNTREATED CHILDREN

	TOTAL		TONSILLITIS		NO TONSILLITIS	
	NO.	%	NO.	%	NO.	%
Treated	247	100	124	50.2	123	49.8
Complete enucleation	(220)	100	(107)	(48.6)	(113)	(51.4)
Incomplete enucleation	(27)	100	(17)	(63.0)	(10)	(37.0)
Untreated	166	100	80	48.2	86	51.8
Total	413	100	204	49.4	209	50.6

49.8 per cent, did not (Table VI). Of 166 children who were not operated upon, 80, or 48.2 per cent, gave a history of recurrent tonsillitis, and 86, or 51.8 per cent, did not. The influence of tonsillectomy on the recurrence of tonsillitis and sore throat showed on analysis 124 case records, 50, or 40.3 per cent, in whom there was recurrence and 74, or 59.7 per cent, in whom there was none. In 107, or 86.3 per cent, enucleation was complete and in 17, or 13.7 per cent, it was incomplete.

The possible importance of complete and incomplete tonsillectomy has been stressed by some observers. In this series tonsillar tissue was left in 27 who were reexamined after tonsillectomy. A comparison of the average number of infections experienced by these children after tonsillectomy showed no difference from those whose tonsils had been completely enucleated.

COMMENT

When the etiological agent, the portal of entrance, and the focus of infection are unknown in a disease, it is difficult to estimate the influence of any one therapeutic measure. This is particularly true of tonsillectomy in its relation to the prevention of rheumatic infection in children.

A summary of the available data on the value of tonsillectomy in this disease is inconclusive for reasons already discussed. It is obvious that before we can expect to obtain results based on conclusive evidence, it is necessary that:

1. The number of cases studied be greatly increased.

2. Criteria for rheumatic infection and disease of the tonsils be uniform.

3. Enucleation of the tonsils be complete and other possible foci of infection be excluded.

4. Cases be so recorded that it may be possible to deduce what has actually been the course of events.

5. The duration of observation be extended.

6. Cases not operated upon be studied as control groups; that such groups be comparable, so far as is possible, to the treated cases, in

respect to age, constitution, duration of observation, virulence of infection, and susceptibility to its recurrence.

This investigation includes a small series of 247 children from whom the tonsils were removed. The results as judged by the occurrence and recurrence of manifestations of infection after operation do not indicate that tonsillectomy is to be advised as a routine therapeutic measure for the prevention of rheumatic heart disease in children. One may urge that this particular series of children was unusually susceptible, that the etiological agent was particularly virulent, or that other foci were still present. The question of incomplete tonsillectomy cannot be discussed from our limited data. Its importance has, we believe, been overemphasized. The impossibility of complete surgical removal of all possible foci in the nasopharynx is obvious. To expect tonsillectomy to prevent the occurrence of rheumatic heart disease does not seem justified in the light of present insufficient knowledge of this disease.

SUMMARY

1. Of 413 rheumatic children observed over a period of from one to ten years, 247 were subjected to tonsillectomy.

2. Manifestations of infection recurred in 47.7 per cent and appeared for the first time in 34.7 per cent of the treated children.

3. In only 17.5 per cent was there no manifestation of rheumatism after the operation.

4. In rheumatic children less than nine or ten years of age, recurrent attacks were frequent, whether or not tonsillectomy had been performed. In older children recurrent attacks became less frequent regardless of enucleation of tonsils.

5. The age at which tonsillectomy was performed and not the fact of tonsillectomy appeared to be the significant factor in the incidence of nonrecurrence of infection after operation.

CONCLUSION

The routine removal of tonsils for the prevention of rheumatic heart disease in children is not based on conclusive data.

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ON THE LYMPH FLOW OF THE HUMAN HEART, WITH REFERENCE TO THE DEVELOPMENT OF THE CHANNELS AND THE FIRST APPEARANCE, DISTRIBUTION, AND PHYSIOLOGY OF THEIR VALVES*

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IN MY researches on the genesis, arrangement and action of the valves in the lymphatic system,† I discovered some notable features respecting their initial appearance and distribution in diverse parts of the human body.‡ In an organ like the lung, for instance, which does not exercise its function until the close of fetal life, the valves arise synchronously with those of the systemic lymphatics—only the ones in the neck and mediastinum appearing earlier. But in the several areas of the lung remarkable differences obtain in the number of valves laid down. In the fetus and newborn they occur abundantly in the pulmonary pleura facing the heart and are somewhat less numerous in that facing the diaphragm and the anterior thoracic wall, but they are absent or at best very scarce at the apex and in the vertebral and the dorsal and lateral costal surfaces of the lung. This strikingly unequal disposal of the lymphatic valves suggests but one explanation, namely, that the excursions of the beating heart, for example, impinging on the medial side of the lung and tending to interfere with the steady flow of lymph during its respiratory expansion, led to the evolution of such regulators whereby the direction of the current is maintained and safeguarded. I believe that this particular illustration of the arrangement of the lymphatic valves represents the most lucid demonstration yet observed of their fundamental purpose.

Such morphological peculiarities as these, and speculations on their physiological significance, induced me to seek information concerning the genetic, as well as functional, history of the lymphatic valves in the heart, especially because this organ is the first permanent one to assume its definite duties in the life of the individual.

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†In 1923, the directors of the Bache Fund of the National Academy of Science made a grant of one hundred dollars, and the committee on grants of the American Association for the Advancement of Science set aside the same sum to aid me in my investigations on the evolution and comparative morphology of the lymphatic system. Since considerable time will still elapse before a comprehensive monograph, which is being prepared, is ready for publication, I take the opportunity here and in other papers dealing with the subject of acknowledging the assistance given in pursuance of that plan.

‡The Genetic History of the Valves in the Lymphatic System of Man, Am. Jour. Anat., 1928, xl, 413.

Further Observation on the Numerical Variability, Position, Function, and Fate of the Valves in the Human Thoracic Duct, Anat. Rec., 1928, xxxviii,

On the Distribution of Valves and the First Appearance of Definite Direction in the Lymph Drainage of the Human Lung, Am. Rev. Tuberc., 1928, xviii, 360.

Three hundred years have elapsed since the rediscovery of the lymphatics by Asselli (1622), and though a goodly array of papers has dealt directly or indirectly with these vessels of the heart, much obscurity still prevails about them. Their origin and differentiation in the human heart, not to mention that of their valves, has never been examined, and regarding their rôle in its activities "physiology is silent," as one author succinctly remarks.

The growth of the knowledge we have of the lymph channels of the heart has been halting. Mascagni, in his famous treatise on the lymphatic system printed in 1784, cites Rudbeck, Nuck, and Cassebohm as having seen them earlier. Cruikshank, whose work was published two years after Mascagni's also confirmed their findings, but all of these investigators had only perceived the superficial lymphatics. Later these pericardial vessels were studied in man and other mammals by Gurlt (1844), Leyh (1859), Teichmann (1861), Eberth and Belajeff (1866), Wedl (1872), Bizzozero and Salvioli (1787), Sappey (1885), Tanasescu (1907), Rainer (1909), and others, so that today we possess an adequate picture of their course and topography. Most of the investigators named also traced the path of the lymph stream from the heart to the nodes of the mediastinal territory. Most recently (1928), Shore has undertaken an inquiry into this phase of the subject from the standpoint of infections.

It is when we turn to the matter of deep cardiac lymphatics that we meet with radical differences of opinion regarding their existence and nature. Leyh (1859), it seems, was the first to point out their presence in the myocardium, and Luschka (1863) described them as forming a rich network discharging into the peripheral plexus at the furrows and apex of the heart. However, Eberth and Belajeff (1866) claimed that the heart muscle was deficient in such vessels. Henle (1868) and Schweigger-Seidel (1871) likened the organ to a "lymphatic sponge," they assuming that all the interstices between and around the fasciculi contained and conveyed lymph. By means of the "Einstich-methode," or injection by puncture, Skwartzoff (1874), Skworzow (1874), and Navalichin (1882) filled a myocardial net of channels which they interpreted as lymphatic, and which they said was lined throughout with endothelium. Salvioli (1878), supported by Masini (1887), could not discern continuity between the lymph vessels of the interfascicular septa and the intermuscular spaces, and hence rejected the simile of the "lymphatic sponge" as applied to the cardiac musculature. On the other hand, Bianchi (1886) was led by experiments to believe that no true lymphatics—that is, vessels possessed of an intima—occur in the myocardium, and that the lymphatic fluid percolates through its ill-defined crevices, eventually to be absorbed by the pericardial channels. A year later, Albrecht (1887), by injecting the living mammalian heart and letting its natu-

ral movements disseminate the injected mass, reached the conclusion that a widespread and endothelial-lined lymph capillary plexus pervaded its muscle. But Ranvier (1889) again revived the idea of the "lymphatic sponge."

In an attempt to settle the controversy, Nyström (1897) employed three methods: those of injection, sectioning, and Golgi impregnation, on fresh hearts of the dog, cat, pig, calf, sheep, rabbit, and man. His inference was that the lymphatic pathways of the heart muscle are composed of a combination of interstitial spaces and true endothelial-lined vessels. The spaces themselves are of complicated form and are in intimate relation to the muscular elements, in so far as they not only surround the individual fibers but also send minute radial extensions into their sarcoplasm. Notwithstanding all the evidence to the contrary, Poirier and Cunéo (1902) returned to Sappey's (1885) earlier attitude of denying altogether the existence of definite lymphatics throughout the myocardium.

The most elaborate and, in my judgment, the most decisive work yet done to demonstrate the actual occurrence and character of myocardial lymphatics was carried out by Bock (1905). Confronted squarely by the pertinent criticism, already recognized by his immediate predecessors, that the results derived from blindly injecting the myocardium by puncture do not permit absolute distinction between lymphatic and hemal plexuses, he made use of the method of double injection. After flushing the blood from the coronary vessels and filling them with carmine gelatine under pressure, and then forcibly injecting Berlin blue into the myocardium, he was able to reveal two complex yet entirely separate vascular networks both possessing distinct walls. He plainly asserts that diffusion of the injecta from one set of vessels into the other was not visible. Nevertheless, Cash (1917), on the basis of a study of the formation of the lymphatics in the heart of the embryo and fetal pig, not only maintained that the myocardial plexus of lymph channels is not as extensive as Bock believed—they becoming fewer and smaller the deeper they penetrate toward the endocardium—but he intimated that Bock did confuse those vessels.

Nor is there unanimity of opinion concerning the existence of lymphatics in the endocardium. Contrary to Eberth and Belajeff (1866) and Wedl (1872) who had reported a plexus of these canals which enter even into the flaps of the mitral and tricuspid valves, Schwartz-Skwartzoff (1872) said he was unable to find them. But Sappey's (1885) injections with mercury did disclose such a network, an observation that was corroborated by Nyström (1897) who also agreed that it flourished better in the ventricles than in the atria. Yet Cash (1917) contends that "claims for an endocardial lymphatic plexus are evidently founded on partial injections of the His bundle." Although I

cannot deny the reality of lymph vessels in the inner lining of the heart, the objection of Cash is warranted. Before the existence of the atrioventricular bundle was known, the channels manifested by injections into it naturally were assigned to the lymphatic system. Indeed, further research has still to prove that the injectable sheaths which follow the intricate ramifications of that conduction bundle are not in direct communication with the true lymphatics.

For the sake of clarity in the account of the arrangement of the lymphatic valves, the following image of the lymph drainage in the

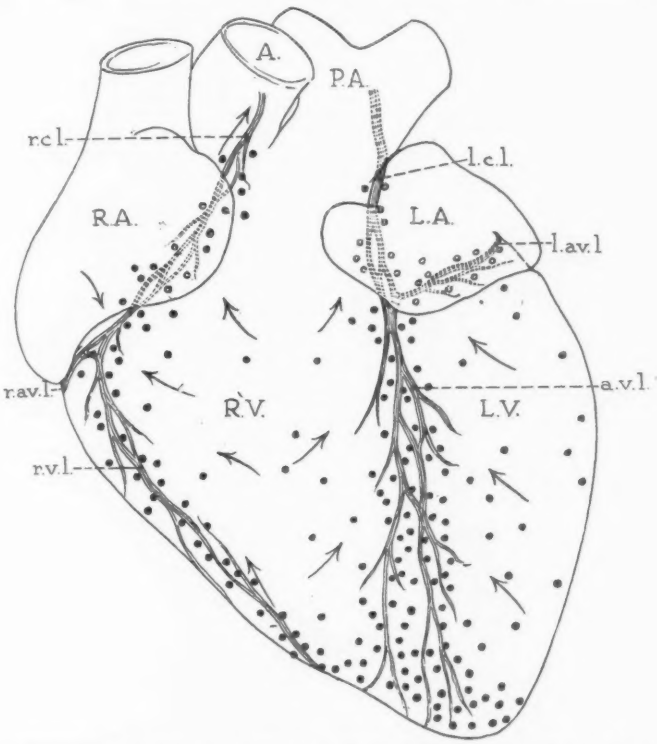

Fig. 1.—Diagram of the anterior surface of the fetal heart, from the middle of intrauterine life, showing the course of the chief channels of the pericardial lymphatic plexus, and the distribution of its values. Approximately 4 X. *R.V.*, *L.V.*, *R.A.*, and *L.A.*, right and left ventricles and atria, respectively; *A*, ascending aorta; *P.A.*, trunk of pulmonary artery; *a.v.l.*, anterior ventricular lymphatic; *r.v.l.*, right ventricular lymphatic; *r.av.l.* and *l.av.l.*, right and left atrioventricular lymphatics; *r.c.l.* and *l.c.l.*, right and left cardiac lymphatics, the efferent lymph ducts of the heart; (It should be stated that these lymphatics are portrayed schematically, no attempt being made to show the great irregularity of caliber and the plexiform character, so characteristic of even the larger lymphatics). The arrows indicate the course of the lymph stream as determined from the directions in which the valves point. The location of the valves, marked by dots, was plotted in a graphic reconstruction.

human heart may be constructed in its main outlines. From the delicate radicles and meshes of a more or less extensive net of vessels spread throughout the endocardium and myocardium, the lymph is collected by the interfascial channels which, closely paralleling the myocardial tributaries of the coronary blood vessels, transport it to

the external layer of the heart. Here, particularly along the furrows, they emerge as relatively large channels the frequency of which, as seen in serial sections of the fetal heart, dispels any remaining doubt about the existence of kindred channels in its depth. The pericardial lymphatic plexus itself, which receives these deep vessels and which is so clearly portrayed in the figures of Sappey and Tanasescu, for example, covers the ventricular district of the heart lavishly, the atrial scantily. In my own diagrams (Figs. 1 and 2) merely the course of the major collecting conduits of this superficial plexus is pictured.

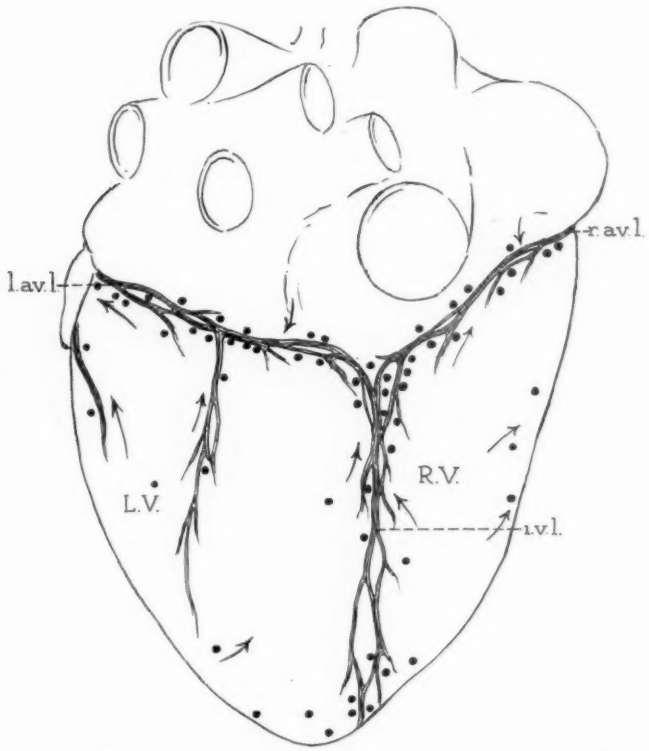

Fig. 2.—Diagram of the inferior or diaphragmatic surface of the heart illustrated in Fig. 1. *i.v.l.*, inferior ventricular lymphatic. Other references as in Fig. 1.

Of these conduits—plexiform and twining about the contiguous coronary arteries and veins—the one (a.v.l., Fig. 1), situated in the anterior ventricular sulcus and draining the greater part of the front of the heart except at the right, unites with the left atrioventricular lymphatic (l.av.l.), running from the diaphragmatic surface, to form the left trunk of the two principal lymphatic outlets of the heart. The efferent (l.c.l.) so formed proceeds upward between the left atrium and the pulmonary arterial trunk, and then bending to the posterior side of the latter traverses in some cases an intrapericardial and retropulmonary lymph node, more rarely a subaortic one, on its way to

the tracheobronchial group of nodes. Similarly a ventricular lymphatic (r.v.l.) drains much of the right ventricle, is joined by an atrioventricular lymphatic (r.av.l.) coming from the rear, and is continued as the right principal lymphatic outlet (r.c.l.) of the heart. This channel passes along the forward side of the ascending aorta to enter an anterior mediastinal node, which in the infant is retrothymic and in the adult is situated at the root of the left common

Fig. 3.—Photomicrograph of part of a transverse section through a 30 mm. (2.2 months) human fetus at the level of the base of the heart. X 27. *r.c.l.* and *l.c.l.*, right and left cardiac lymphatics, representing the primary lymph channels invading the heart during development, and retained throughout life as the efferent ones. *t.d.*, thoracic duct; *t.l.*, pretracheal lymphatic plexus; *R.A.* and *L.A.*, right and left atria; *A*, ascending aorta; *P.A.*, trunk of pulmonary artery; *S.V.C.*, superior vena cava; *b.*, bronchi; *oe*, esophagus; *a*, descending aorta.

carotid. In few instances the right trunk on leaving the heart bears a small intrapericardial node, preaortic in position (Tanasescu). It is evident that variations occur; for example, the right trunk may occasionally (3 per cent) go behind the pulmonary artery to combine with the left trunk.

Since the literature is mute on the development of the lymphatics in the human heart, it was necessary to determine the first appearance and situation of these before considering that of their valves. In an embryo of 30 mm.—at the end of the second lunar month of pregnancy—two plexiform extensions from the mediastinal lymphatics have entered the base of the heart. One, arising as a branch from the upper reaches of the thoracic duct, near the junction of this duct with the left jugular lymph sac, and extending down in front of the left carotid and to the left of the aortic arch, comes to lie (r.c.l., Fig. 3) in the groove between the pulmonary artery and the ascending aorta. It then grows out ventral to this vessel and along the right coronary artery, although in the 30 mm. specimen it had made little progress here, its tip soon vanishing in the mesenchyma. The other extension (l.c.l.), the more important of the two and a derivative of the pretracheal lymphatic plexus, runs dorsal to the pulmonary artery and then to its left, subsequently to be prolonged along the left coronary artery. The pretracheal plexus itself largely represents a downward growth from the right jugular lymph sac by the side of the right cardinal vein, though it is also in anastomotic connection with projections from the thoracic duct.

The two original or primary lymphatic extensions into the embryonic heart are retained as the efferent lymph passages of the adult organ. Though there is nothing to prevent the cardiac lymph stream from taking its way to the lymphaticovenous gateways at either the right or the left jugulosubclavian regions, it seems the pathway to the right via the tracheal plexus and the right bronchomediastinal trunk assumes greater significance.

In the 40 mm. human embryo the primary lymphatics of the heart have extended far along the coronary arteries in the interventricular and atrioventricular sulci. Because of the limited human embryonic material available, I was unable to ascertain how the formation and elongation of the earliest cardiac lymphatics are achieved, whether by centrifugal sprouting or by the centripetal coalescence and addition of discrete lymphatic spaces, as happens in the genesis of the main systemic conduits. It may be pointed out, however, that the mesenchymal tissue in the furrows is wider and of looser texture than elsewhere in the visceral pericardium.

During the third month of intrauterine life a net of lymph vessels expands rapidly over the periphery of the heart so that by the beginning of the fourth month the greater part of the surface is furnished with them. Ultimately this pericardial plexus becomes intricate and close-meshed over the ventricular territory, but always remains more restricted and simple over the auricular.

In his study of the development of the cardiac lymphatics in the pig, Cash noticed that the superficial plexus is established almost com-

pletely before the invasion of the myocardium commences. His endeavor to inject the myocardial lymphatics in specimens ranging from 60 to 150 mm. in length failed to reveal many such vessels. Indeed, he implies the conclusion already touched upon that neither are they as abundant in the myocardium as Bock supposed nor do they appear in the endocardium—a view which I am not prone to accept.

At the end of the third or the beginning of the fourth month of prenatal life, the first valves have their inception in the developing pericardial lymphatic plexus. The earliest ones arise in the main channels accompanying the coronary blood vessels. Shortly after, during the multiplication of connections in the network and its differentiation, in which the abandonment and collapse of some channels and the increment of others is dominant because of the shifting hydrostatic conditions ensuing from the active development and growth of the heart as from that of any other organ, valves spring up also in the more distant parts of the plexus.

Despite the early demands put on the heart in the formation of the individual, its finished state is accomplished no earlier, it seems, than that of most other organs. Certainly this holds true as regards the acquisition of its lymphatics and their valves, in which process it does not even surpass the lungs. To say that during ontogenesis the details of organization are engendered in conformity with some determinate pattern or memory inherent in the protoplasm is to mask our ignorance; yet it is impressive that such creation occurs irrespective apparently of immediate functional exigency. The cells that build the lymphatic system are capable of proliferating valves between the end of the second and the beginning of the fifth month of fetal life and probably lose that power thereafter. The oldest or earliest lymphatic territory acquires its valves first. I have shown previously* that at approximately two months some have already appeared in the tributaries of the jugular lymph sac in the neck region. As early as three months they are encountered in such a distal area of the body as the femoral trigone, and but a short while after they abound throughout the lymphatic plexus of the entire lower extremity. It is at this time too that they are generated in the heart and lungs.

In their mode of origin and development the valves of the cardiac lymphatics do not differ from those elsewhere in the body. For a detailed description of the genetic procedure the reader is referred to my paper in the *American Journal of Anatomy*.† It suffices to say that, in the large systemic trunks like the thoracic duct, their inception and perfection is identical with that of the venous valves,‡

*Loc. cit., footnote, page 210.

†Loc. cit., footnote page 210.

‡Otto F. Kampmeier and Carroll La Fleur Birch: The Origin and Development of the Venous Valves, With Especial References to the Saphenous District in Man, Am. Jour. Anat., 1927. xxxviii, 451.

whereas in the peripheral plexuses including those of the heart, lungs, etc., it varies according to whether they originate at confluences of vessels already completed, or at confluences just being established. In the one case the valve issues from an endothelial proliferation that encircles the entrance of one channel into another, in the other the valve is produced from the tip or bud of a small vessel that grows at a tangent into the lumen of a bigger vessel. An example of a fully

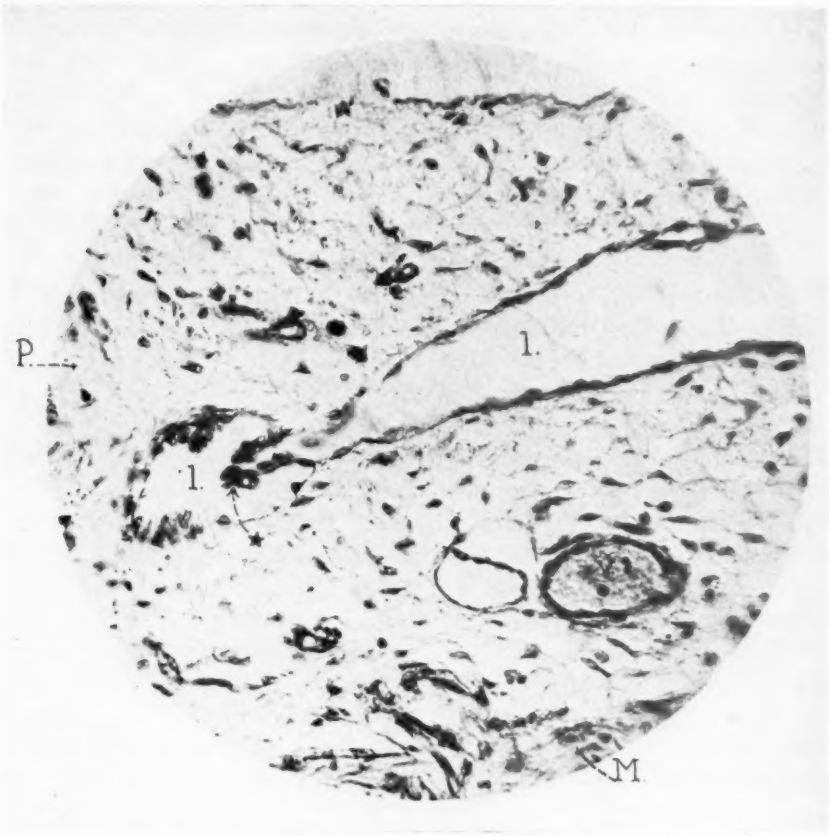

Fig. 4.—Photomicrograph of a section at the surface of the ventricular portion of the heart in a fetus of 105 mm. (3.8 months). X 270. *P*, pericardium; *M*, outer margin of myocardium; *l*, lymph vessels, with a valve at *; *V*, branch of a coronary vein.

formed valve in the pericardial lymphatic plexus is depicted in longitudinal section in Fig. 4 (at *).

When we look at the distribution of the lymphatic valves in the heart, we find that the larger channels of the pericardial plexus are supplied more liberally with them, as we should expect, than the more terminal meshes. Curiously, too, they are more plentiful on the anterior than on the inferior or diaphragmatic face of the heart. Comparatively, they are most numerous at the apex where the larger

conduits of the network are in direct union. It is true that these observations were made on the fetal organ, but there is evidence to favor the assumption that the production of lymphatic valves is finished before birth and that their relative numerical differences on the several sides of the heart persist. With few exceptions all of the valves were found in the ventricular portion. For example, of the nearly 300 valves counted in the heart of a 105 mm. (3.8 mo.) fetus, not more than four or five occurred on the atrial surface. In the depth of the myocardium they were absent, but near its periphery an occasional one was seen in the mouths of the interfascial lymph channels pointing outward to the pericardial.

In approaching the physiological side of the subject, it is obvious first of all that the direction in which the flaps of the valves project is indicative of the direction of the current. From the disposal of these structures it is correct to infer that the flow is from the depth of the heart to its exterior, thence through channels located in the furrows into the efferent lymphatics leaving the heart, and, after filtering through one or more lymph nodes, into ducts already mentioned that carry it to the venous stream.

A comparison of the lymphatic organization of the lung and heart—two organs so totally dissimilar structurally, functionally, and in the periods of their initial activtiy—shows that the influences which the valves are designed to counteract are situated in the one case outside, and in the other within the organ. While the peculiar distribution of the valves in the lung, as briefly sketched in the introductory paragraph, is the answer to the movements and pressure of the heart, diaphragm, etc., upon it, in the heart the dominating factor is its own musculature, hence the great preponderance of valves on the ventricles.

Similarly, the site of the chief lymph channels in the furrows of the heart like that of the other coronary vessels is without doubt an adaptation to the architectural arrangement of its fascicles and the manner of its pulsation. Analogous to the wringing out of a wet cloth, the kind of contraction brought about by the spiral twist of its muscular bundles—fastened as they are to the fibrous rings of the venous and arterial ostia at the base of the heart and converging at the apex in a vortex—not only effectually evacuates the blood from the ventricular chambers, but also greatly compresses the vessels within their walls. During systole the muscular force together with the pressure of the blood against the endocardium squeeze the lymph from the substance of the heart to its surface. This is facilitated by the relaxation of the pericardial covering and the consequent augmentation in the volume content of its lymph channels occurring when the ventricular diameter diminishes during the beat. It is evident that the extensiveness of the superficial lymphatic plexus is the expression not of any vigorous metabolism within the connective tissue

of the pericardium itself, but of service as a lymph reservoir in close periodic sequence.

The expulsion and outflow of lymph from the heart through the two efferent pathways probably occurs in a continuous stream, for both systole and diastole sustain it, the first because of the shortening of the heart axis from apex to base, the second because of the stretching of the pericardium during the filling of the chambers. Yet during both phases factors arise which also favor backflow in its lymphatics. With the distention of the ascending aorta and the pulmonary artery during ventricular systole and the subsequent closure of their semilunar valves, the adjacent thin-walled lymph vessels would be affected because of their close juxtaposition to them. In the second place, the slackening of the myocardium in the diastolic phase, causing a suction-like action on its vessels, would entail a retrograde motion of the lymph were it not for the interposition of the numerous valvular barriers.

The lymphatics of the heart must be considered as constituting primarily a drainage system carrying away the products of cellular metabolism not selected by the venous capillaries. A few years ago, Pratt (1924) advanced the suggestion that those lymph vessels may serve a nutritive function, imbibing materials from the blood through the endocardium and conveying them to the heart muscle, thus aiding the coronary arterial stream—an hypothesis for which there is little foundation. True, the lacteals absorb foodstuffs through the intestinal lining, yet they do not secrete them again but transport them to the veins for diffusion to the entire organism by the blood stream.

SUMMARY

1. Despite the many papers that have been published on the lymphatics of the heart, much obscurity still prevails concerning their existence in the endocardium and their extent in the myocardium.

2. Because neither the development of the channels in the human heart, nor that and the distribution of their valves have been studied before, the present communication aims to offer information in this matter.

3. At the end of the second lunar month of intrauterine life, two plexiform extensions from the mediastinal lymphatics have entered the base of the heart. One, arising from the upper reaches of the thoracic duct and passing down in front and to the left of the aortic arch, comes to lie between pulmonary artery and ascending aorta and then grows ventral to the latter and along the right coronary artery. The other, a derivative of the pretracheal lymphatic plexus runs behind and to the left of the pulmonary artery to be prolonged along the left coronary artery. Both of these primary channels are permanently retained to constitute the efferent lymph conduits of the heart.

During the third month a net of vessels growing out from them expands rapidly over the periphery of the heart. While that of the ventricular territory eventually becomes intricate and close-meshed, that over the auricular remains less well-developed. Extensions from this superficial or pericardial plexus invade the myocardium to form its plexus.

4. At the end of the third or the beginning of the fourth month of prenatal life, the first valves have their inception in the developing pericardial lymphatic plexus, especially in the main pathways accompanying the coronary vessels; subsequently, they spring up also in the more distant stretches of the network, but in smaller numbers. Their mode of genesis—similar to that in other peripheral lymph channels of the body—varies according to whether they originate at confluences already completed or at confluences just being formed. In one case the valve arises from an endothelial proliferation that encircles the entrance of one vessel into another; in the other, it is produced from the tip or bud of a small vessel that grows at a tangent into the lumen of a bigger vessel.

5. Regardless of the early demands put on the heart in the life of the individual, it acquires its perfect lymphatic organization no earlier than any other organ or region, with the exception of the jugular and mediastinal districts in which the earliest valves make their appearance at two months. In this respect, the heart does not even surpass an organ like the lung which is not called upon to serve until birth.

6. As to distribution, more lymphatic valves are found on the anterior side than on the diaphragmatic side of the heart, at any rate in the fetus. With few exceptions all of these valves occurred on the ventricular portion; for example, of the nearly 300 valves counted in the heart of a 3.8 mo. fetus, not more than four or five were atrial in location. In the depth of the myocardium these structures are absent.

7. Finally, the physiology of the lymph circulation of the heart is discussed: the direction of its flow, the mechanical factors influencing it, and its function.

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COMPARISON OF THE ELECTRICAL AXIS SHOWN BY THE ELECTROCARDIOGRAM WITH ROENTGEN MENSURATION OF THE HEART*

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DETERMINATION of the electrical axis (formerly spoken of as the presence or absence of a right or left ventricular preponderance) is part of the routine analysis of electrocardiograms. Deviation of the electrical axis was formerly considered reliable evidence of preponderating enlargement of the right or left ventricle according as the deviation was to the right or left. More recently, however, the work of Cohn[1] and others, and especially that of Herrmann and Wilson,[2] has shown that the electrical axis may be made to deviate from the normal by the position of the heart in the thorax, and by the manner in which the excitation is conducted through the specialized tissue in the ventricles, as well as by change in the relative weights of the right and left ventricles. Herrmann and Wilson compared the electrocardiographic data with the weights of the ventricles separately dissected post-mortem from the remainder of the heart. They found that deviation of the electrical axis and preponderating hypertrophy of right or left ventricle by this method of separate weighing were not in agreement except in instances in which the dissected mass of the ventricles, not the entire heart, weighed in excess of 250 grams. In discussing their work Lewis[3] states that electrical curves cannot be read as indicating preponderating hypertrophy of one or the other ventricle unless independent evidence of very definite cardiac hypertrophy exists; even so, the lie of the heart and the possibility of defective conduction in branches of the A-V bundle may need to be taken into account.

It is my opinion, however, that there is yet a tendency to place too much reliance upon a deviation of the electrical axis as indicative of preponderating hypertrophy of one or the other ventricle. In view of this opinion and the change in the interpretation of the electrical curves which the above-mentioned work demands it was considered desirable to compare the electrical axis with the results of roentgen mensuration of the heart. The latter is considered by most clinicians as the most reliable method of detecting enlargement of the heart in the living patient. Accordingly 100 successive cases, examined in the Heart Laboratory of the Evans Memorial, were selected for checking

*From the Evans Memorial.

of the electrocardiographic evidence of cardiac hypertrophy with the results of roentgen mensuration. All of the roentgen plates were taken at a distance of 6 feet, a suitable distance for teleroentgenography. The electrical axis in the electrocardiograms was determined by the method of Dieuaide.[4]

RESULTS

Number of cases	100
1. Agreement	67
2. Disagreement	23
3. Questionable	10

1. In the 67 cases in which agreement was found the electrical axis and roentgen findings were normal in 60, while in 7 cases the electrocardiogram disclosed left axis deviation and the radiograph enlargement of the heart, more marked of the left ventricle.

2. In the group of 23, in which the data were at variance, the roentgen findings were normal in 21 although axis deviation was present in the electrocardiogram; in two patients the reverse conditions were found. The angle of the axis in the 21 cases measured as follows: –1° to –9°, 2 cases; –10° to –19°, 7 cases; –20° to –29°, 4 cases; –30° to –39°, 3 cases; –40°, 1 case; –57°, 1 case; and +115°, +125°, +150° in the other 3 cases.

3. In the group of 10 patients in whom it was open to question whether the x-ray and electrocardiographic data pertaining to cardiac hypertrophy were in disagreement, the electrical axis was normal in nine and the roentgen findings as follows: symmetrically enlarged, 3; enlarged, especially the left auricle, 1; dilated left auricle, 3; dilated right auricle, 1; and slightly enlarged auricles, 1. In the tenth case the axis measured –12° and the x-ray showed doubtful enlargement, with the heart lying more horizontally due to obesity of the patient.

It is well known that in electrocardiograms taken of enlarged hearts the electrical axis is not deviated to right or left unless the enlargement of the heart is of the type in which either right or left ventricle shows preponderance. Therefore, the normal axis found in the first three of the questionable group merely illustrates a limitation in the electrocardiogram.

In 7 cases the x-ray disclosed enlargement of one or both auricles. The P-wave in Lead II in these cases measured 0.15, 0.15, 0.15, 0.20, 0.20, 0.25, and 0.28 millivolts, respectively. Only the last two figures are suggestive of auricular hypertrophy.

There were 18 cases in which enlargement of the heart was disclosed by x-ray. In 7 of these cases, left axis deviation was present; in 2 the axis was normal. In 4 the enlargement was symmetrical so that the

normal axis in the electrocardiogram could be predicted, and in the remaining 5 cases of this group the roentgen data indicated enlargement of one or both auricles alone; in this last 9 cases the electrical curves are not expected to indicate cardiac enlargement.

Deviation of the electrical axis was present in 29 electrocardiograms, but the roentgen findings indicated enlargement of the heart in but 7 cases. In one other there was a questionable enlargement, and in the remaining 21 cases the x-ray examination disclosed a normal sized heart.

If one eliminates the 60 cases in which there was no enlargement and the 5 in which the enlargement was limited to the auricles, there remain 35 cases in which the electrical axis or the roentgen mensuration indicated enlargement. The percentage of agreement of the two methods of examination is shown in Table I.

TABLE I

		NUMBER	PER CENT	
Electrocardiogram + / X-ray +		7	20	
Electrocardiogram + / X-ray 0		21	60	77%
Electrocardiogram 0 / X-ray +		6	17.1	77%
Doubtful		1	2.9	
Total		35	100	

This work was repeated substituting the "Index"[5] for the electrical axis determined by the method of Dieuaide; the results were about the same by the two methods.

SUMMARY

Deviation of the electrical axis in the electrocardiogram has been shown to be unreliable evidence of preponderating hypertrophy of one or the other ventricle unless the weight of the latter exceeds 250 grams. The position of the heart in the thorax and the possibility of abnormality in the conduction of the impulse through the branches of the bundle of His must be considered.

If the above statements are correct, it is believed that there is yet a tendency to place too great reliance on the electrical curves in the diagnosis of preponderating hypertrophy of one or the other ventricle.

A series of one hundred successive cases have been selected for checking the electrocardiographic evidence of cardiac hypertrophy with the results of roentgen mensuration.

The indications of cardiac enlargement disclosed in the two methods of examination were found to agree in 67 cases, to disagree in 23, and to be questionable in the remaining 10.

In most of the cases in which the results were at variance, the numerical value of the electrical axis indicated a deviation to the right or left although the x-ray disclosed a normal sized heart. Values of the axis as far from the normal (0°–90°) as –40°, –57°, +125°, and +150° were found in this group.

It has long been known that the electrical curves do not disclose symmetrical enlargement of the heart; one ventricle must be enlarged out of proportion to the other.

Enlargement of the auricles, as disclosed in a small group of the radiographs, was not reliably indicated in the electrocardiograms.

In 7 of the 9 cases in which the x-ray showed an asymmetrical enlargement of the heart the electrocardiogram showed a deviation of the electrical axis.

In but 7 of the 29 instances of axis deviation shown in the electrocardiogram did the roentgen examination disclose an enlarged heart.

The percentage of disagreement of the two methods of examination in the 35 cases in which one or the other indicated cardiac enlargement was 77 per cent.

CONCLUSIONS

Deviation of the electrical axis in the electrocardiogram is an unreliable means of determining preponderating hypertrophy of one or the other ventricle.

The interpretation of the character of the waves in an electrocardiogram as indicative of ventricular hypertrophy should require confirmation by the results obtained by other methods of examination, namely, physical and radiographic.

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Department of Clinical Reports

PLEURAL EFFUSION LOCALIZED IN AN INTERLOBAR SPACE*

Report of a Case of Heart Failure Together With Autopsy

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PLEURAL effusion associated with congestive heart failure is observed very frequently, but the localization of fluid in an interlobar space in this state is very unusual. The recognition of the fact that it occurs is important in the differential diagnosis of shadows seen in the x-ray photographs of the chest. It is for this reason that the case of a patient exhibiting this sign is reported.

CASE REPORT

I. P.† (Hospital No. 5869), a female, sixty-four years old, was first admitted to hospital on February 12, 1927, complaining of shortness of breath and a sensation of oppression over the heart for six months, and edema of the legs for five days.

The family history was negative.

Past History.—The past history was negative. She had had only measles, mumps, and whooping cough in childhood. She never had acute rheumatic fever, was not subject to attacks of tonsillitis, and was well until the onset of present illness.

Present Illness.—In August, 1926, the patient experienced shortness of breath on exertion. Shortly after this she began to suffer from palpitation; she went to a physician who discovered an affection of the heart, and prescribed digitalis. After taking the drug for several weeks without experiencing improvement she discontinued its use. She also stopped going to the physician. Although she became progressively worse in the next three to four months she did not consult another physician until three days before admission to this hospital. For six months she had experienced at times a feeling of oppression over the precordium. When this sensation was present, she had to sit up in bed to catch her breath. Five days before admission she noticed edema of the feet for the first time. During the next two days this increased, extending up beyond the knees. She then called a physician. She went to bed and was given a milk diet. Although edema decreased very rapidly, her physician advised removal to this hospital.

Physical Examination.—The patient was a well-developed, well-preserved woman. She was slightly dyspneic and slightly cyanotic. She coughed occasionally. The pupils were regular and equal; they reacted to light and in accommodation normally. There was slight arcus senilis. There was slight exophthalmos. The eye-grounds were normal except for slight tortuosity of the retinal vessels. All the teeth were present except one molar. The tonsils were enlarged and cryptic. There

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†We wish to thank Dr. Otto V. Huffman for referring this patient to us.

was no tracheal tug. The veins of the neck were distended. On percussion the heart was found to be enlarged. The point of maximal impulse was felt in the sixth interspace, 12.5 cm. from the midsternal line. There were no thrills and no shocks over the precordium. The rhythm of the heart was regular except for occasional ventricular premature contractions; the rate moderately fast. At the point of maximal impulse the first sound was replaced by a soft systolic murmur transmitted to the axilla, the second sound was faint but clear. Over the base the first sound was replaced by a loud rough murmur, the second sound was clear. A diastolic murmur could not be heard. The radial arteries were thickened and slightly tortuous. There was no capillary pulse. There was slight clubbing of the fingers. The systolic blood pressure was 124 mm. of mercury and the diastolic, 70 mm. There was slight dullness at the base of the right lung posteriorly, and the breath sounds were slightly suppressed. Over both bases posteriorly there were many moist bubbling râles extending up as far as the angles of the scapulae. The liver was enlarged. There was free fluid in the abdominal cavity, and slight pitting edema of the legs and ankles.

The count of the white blood cells was 7,400. Of these cells 64 per cent were polymorphonuclear in form. The count of the red blood cells was 4,900,000. The oxygen capacity of the venous blood was 7.56 mm., which is equivalent to 91.5 per cent hemoglobin. The electrocardiogram showed normal sinus rhythm; the conduction time was normal; left ventricular preponderance was present. The Wassermann reaction in the blood was negative. There was a very faint trace of albumin in the urine; the sediment showed a few leucocytes and epithelial cells on microscopical examination. After the patient was free of all signs of heart failure, the phenolsulphonephthalein excretion was 64.8 per cent in two hours and the Van Slyke index of urea excretion was 37.8. A 2-meter x-ray plate of the chest showed the heart to be enlarged. There was slight clouding at both lung bases. On examination of the x-ray photograph of the chest taken at a distance of 42 inches, a shadow was seen in the chest on the right side at the level of the interlobar line. The shadow extended to the ribs laterally but was entirely free from the shadow cast by the heart medially (Fig. 1, January 13, 1927). It measured 5.3 cm. by 5.0 cm. It was sharply outlined. On physical examination it was not possible to detect signs over the area corresponding to the location of this shadow.

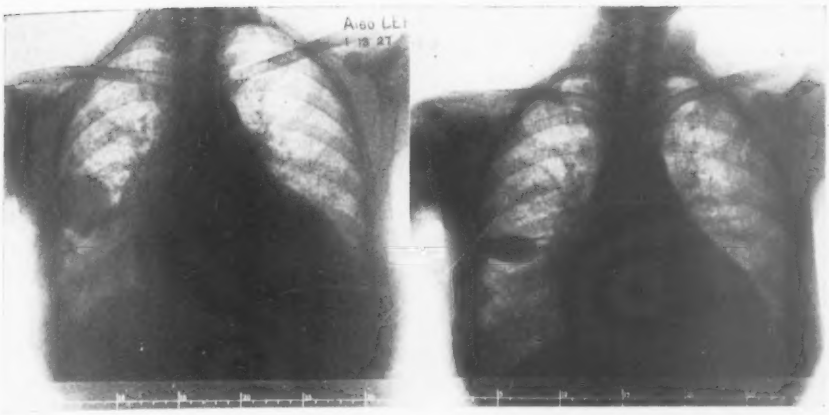
The diagnosis* in this patient was: *Etiological:* arteriosclerosis; *Anatomical:* hypertrophy of the heart, chronic myocarditis, mitral insufficiency, aortic roughening, left ventricular preponderance; *Physiological:* normal sinus rhythm, ventricular premature contractions, congestive heart failure.

We thought the shadow in the right chest was cast by a localized collection of fluid due to heart failure. The patient was admitted to hospital on four occasions, and on each of these the shadow was present and appeared to be one of the manifestations of congestive heart failure. It is with the changes in this shadow that this paper is concerned.

Course in Hospital.—While resting in bed and taking 1200 c.c. of fluid a day the edema decreased. At the end of a week, however, her condition became stationary. She was then given digitan (Merck) 1.0 gm.† within twenty-four hours. This produced changes in the T-waves of the electrocardiogram. There was prompt

*This diagnosis conforms to the nomenclature for cardiac diagnosis approved by the American Heart Association. AM. HEART. JOUR., 1926-27, ii, 202.

†One gm. of the preparation was required to alter the T-wave of the electrocardiogram and to reduce the ventricular rate in auricular fibrillation.



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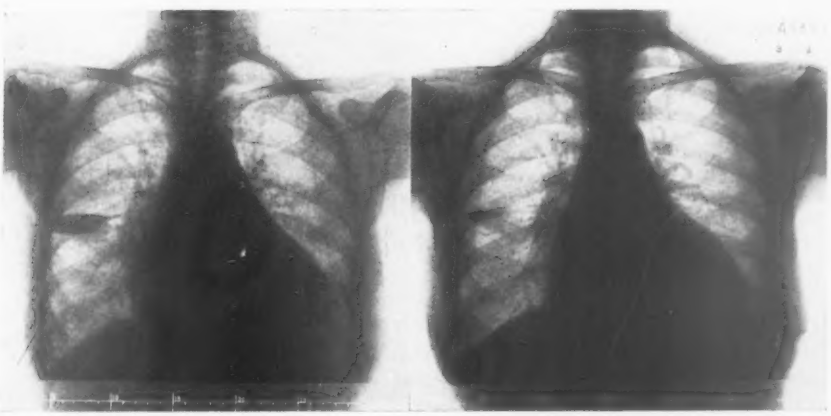

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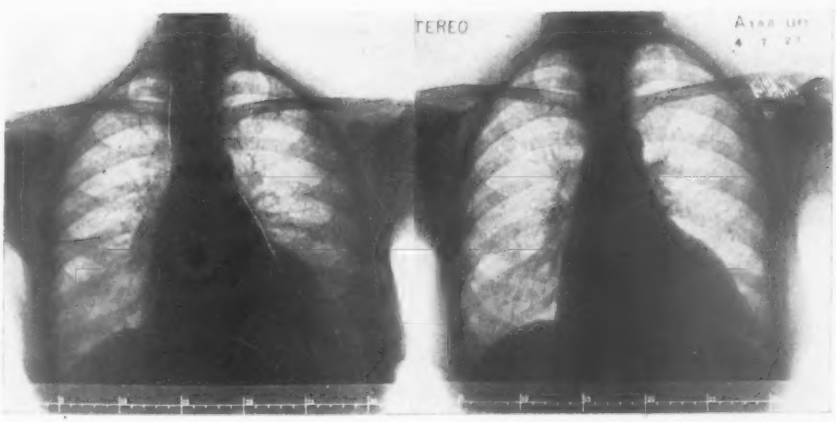

Mar. 18, 1927 Apr. 7, 1927

Fig. 1.—In this figure are reproduced x-ray photographs of the chest taken at a distance of 42 inches. These photographs were taken during the patient's first admission to hospital. The series shows a progressive decrease in the size of the shadow in the chest on the right side. In the last photograph (April 7, 1927) it can no longer be seen.

diuresis. In the next three weeks the dyspnea decreased, the edema disappeared, the ascites decreased, the râles decreased in number, and the liver could no longer be felt. During this time the weight decreased from 54.2 kg. to 47.7 kg., about half of this loss occurring in the course of the first four or five days. During this time the size of the shadow in the right chest did not change.

On the night of February 8, the patient complained of persistent precordial pain. There were no new signs on physical examination. On the evening of February 9, the temperature rose to 102.4° F. (rectal). She was apprehensive and looked ill. She complained of shortness of breath. She coughed. The leucocyte count was 6,000. A blood culture taken at this time remained sterile. The sputum contained no pathogenic organisms by culture or on mouse inoculation. There was no change in the form of the electrocardiogram. On February 10 the temperature rose to 103.7° F., but fell again to normal and remained there. An x-ray photograph taken on February 10 showed that the shadow in the right chest had decreased very much in size (Fig. 1, February 10, 1927), and on February 11 (Fig. 1) and 13 decreased still further. On February 14 the temperature rose again to 101.4° F., and on February 15 the count of the white cells was 11,000. For the next two weeks there were occasional slight rises in temperature above normal. On February 15 and 17 the shadow was still smaller. On February 18 the patient received digitan, 1.0 gm. within twenty-four hours. This was followed by a slight decrease in body weight. By February 23 she was coughing less frequently and ascites had disappeared. There were still a few râles at the pulmonary bases posteriorly. The shadow was seen to be still decreasing in size when photographs were made on February 21, 23, and 26. On February 28 râles could no longer be heard. An x-ray photograph taken on March 3 revealed that the shadow was reduced to a narrow band (Fig. 1). By March 10 the band was still narrower, and by April 7 the shadow had disappeared. The patient was discharged on April 9. She was directed to continue taking digitalis and to limit her fluid intake to 1200 c.c. per day.

On April 27, the patient returned to the hospital for examination. The shadow was again present in the right side of the chest. She had been indulging in more exertion than had been recommended.

On May 7 the shadow had increased still further in size; the patient was readmitted to the hospital for the second time. Except for enlargement of the liver there were no other signs of heart failure. Diuresis occurred promptly when she was given digitalis; the size of the shadow became smaller and finally disappeared (June 1). The patient was discharged. During this admission a rise in temperature did not occur.

On July 8 the shadow had returned again. There were no other signs of heart failure except the presence of the shadow. She was advised to continue taking digitalis and to limit her activities during the summer. On October 14 the shadow was larger. The rhythm of the heart had changed to rapid auricular fibrillation. She went to bed at home and began taking digitalis. On October 18 she was readmitted for the third time. There was slight congestion at the bases of the lungs, the liver was enlarged and there was slight edema of the extremities. Auricular fibrillation was still present. The shadow was larger. She was given digitalis. The volume of urine increased; she became free of the signs of congestive heart failure, and the shadow practically disappeared. She left the hospital on November 8.

The patient was readmitted to the hospital on March 6, 1928, for the fourth time. Heart failure had proceeded much further than on previous admissions. There was marked edema of the extremities extending up to the waist, as well as marked ascites, enlargement of the liver, congestion of the lungs, marked cyanosis

and dyspnea. She had been in this state since January, 1928, but did not wish to enter the hospital. Auricular fibrillation was still present. X-ray examination showed that the shadow was again present. She had been taking digitalis and the ventricular rate was moderately slow. She was given 1200 c.c. of fluid per day for a few days, but did not improve nor did diuresis occur. She was given theocalcin (Merck), 4.5 gm. a day. On the second day of its administration diuresis began. In nine days she lost more than 7.0 kg.; the diuresis at times was more than 3000 c.c. per day. Edema and ascites decreased. There was, however, no change in the size of the shadow. Theocalcin then became less effective and was discontinued. She had not been given digitalis since admission and the ventricular rate was more rapid. The administration of digitan, 1.2 gm. within twenty-four hours, was followed by decrease in ventricular rate; there was, however, no increase in the amount of urine. We continued to give small doses of digitalis in order to keep the ventricular rate slow. During the next weeks theocalcin was given as long as diuresis occurred; when the volume of urine decreased, it was discontinued for a few days. She lost weight and became almost free of the signs of congestive heart failure. The patient now exhibited very frequent ventricular premature contractions. Later, long paroxysms of ventricular paroxysmal tachycardia occurred, while in the intervals between paroxysms there were many ventricular premature contractions. Quinidine was given, but frequent ventricular premature contractions continued to be present interspersed with long runs of ventricular paroxysmal tachycardia. The rapid rate could not be controlled either by the omission of or by the administration of digitalis. The patient grew worse rapidly and died on May 3, 1928. In the x-ray photograph taken on April 26, 1928, the shadow was still present and its size was unchanged.

SUMMARY OF AUTOPSY

Macroscopical Diagnosis.—Calcification and stenosis of the aortic valves; malformation of the aortic valves; cardiac hypertrophy; advanced atherosclerosis of the aorta; moderate atheromatosis of the aortic cusp of the mitral valve and of the coronary vessels; atherosclerosis and infarcts of the kidneys; ascites; edema of the legs and intestines; serous pericarditis; serofibrinous pleurisy of the left cavity with few old adhesions; *obliteration of the right pleural cavity with the exception of a small space between the upper and middle lobes, which was filled with serofibrinous fluid;* pleural induration over both apices; osteoporosis of the sternum.

Microscopical Diagnosis—Heart: Calcification of the aortic valves; old endocarditis (?) and pericarditis of the left auricle; atheromatosis of the aortic cusp of the mitral valve. Aorta: Calcifying atherosclerosis of the intima in the thoracic portion and of intima and media in the abdominal portion of the aorta. Renal arteries: Calcifying atherosclerosis. Lungs: Adhesive pleurisy of the right cavity; purulofibrinous pleurisy in the space between the right upper and middle lobes; serofibrinous pleurisy of the left pleural cavity with purulent lymphangitis; chronic passive congestion; arteriosclerosis. Liver: Atrophic induration and chronic passive congestion. Kidneys: Arteriosclerosis; healed infarcts; passive congestion. Spleen: Passive congestion. Adrenals: Passive congestion. Mesenteric lymph nodes: Sinus catarrh.

Attention at autopsy naturally centered on the right pleural cavity, but the heart was also found to be of especial interest.* The right

*The complete autopsy report and description of the heart will be reported more fully in another paper (Ehrich and Stewart).

lung was adherent throughout to the parietal pleura (Fig. 2), so that the right pleural cavity was completely obliterated. To remove the lung it was necessary to dissect the parietal pleura from the chest wall. The three lobes were adherent to each other, except for a small area at the lateral margin between the upper and middle lobes (Fig. 2). This cavity was filled with pale yellow fluid which was slightly turbid. This location corresponded to that of the shadow which was

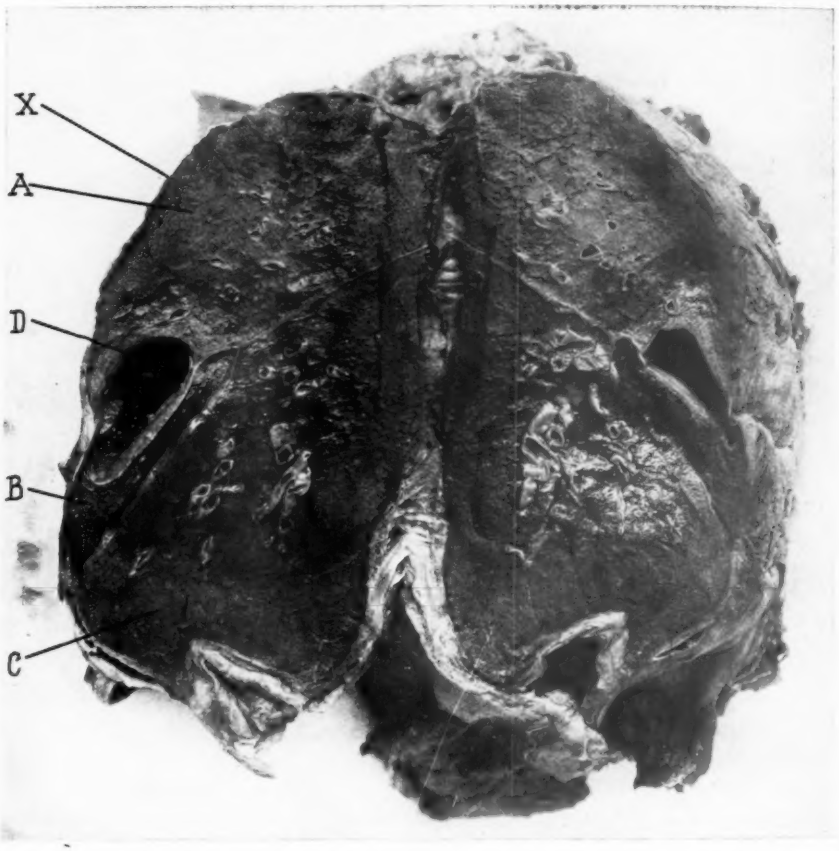

Fig. 2.—In this figure is reproduced a photograph of the right lung on section. *A*, is the upper, *B*, the middle, and *C*, the lower lobe. The space (*D*) between the upper and middle lobes was filled with fluid. The visceral and parietal pleurae were adherent and formed one thick layer *X*.

seen in the x-ray photographs of the chest. On microscopical examination the pleura of the right lung was thickened and connective tissue was abundant. It was adherent to the parietal pleura. The pleura lining the cavity between the upper and middle lobes was thickened and contained large numbers of round cells and polymorphonuclear leucocytes. It was covered with masses of fibroid tissue in which were many polymorphonuclear leucocytes and a smaller number of round

cells. A number of gram-positive cocci were found here, lying partly in couples and partly in chains.

The heart was very much enlarged. There was atheromatosis of the aortic cusp of the mitral valve. There was marked calcification of the aortic valves and the aortic opening was almost obstructed by large rough calcified masses.

The lesion of the heart was apparently that of primary atherosclerosis. The right pleural cavity was entirely obliterated, with the exception of a small space between the upper and middle lobes of the right lung, which was filled with fluid. The gross and microscopical examination did not throw light on the etiological process which was responsible for this state.

COMMENT

The shadow just described was thought to be due to a localized collection of pleural effusion in congestive heart failure, the fluid occupying the space between the upper and middle lobes of the right lung. The position in the x-ray photographs corresponded with this location. Although pleural effusion is one of the most frequent manifestations of congestive heart failure, localization, such as occurred in this patient, is rare. The reason for the sharp localization could not be definitely known when the patient first came under observation. The shadow could, of course, have been caused only by fluid since it disappeared so completely and so quickly and recurred with each attack of heart failure. Adhesion of the visceral and parietal layers of the pleura left, it was thought, only a small free space between the two lobes in which fluid could collect.

When the shadow was first discovered, it was difficult to decide what was casting it. The smoothness of its outline and the absence of metastatic foci were against its being due to a newgrowth. There was no evidence of the presence of pulmonary tuberculosis upon which a diagnosis of localized pleurisy with effusion could be made. The x-ray photographs were not incompatible with a diagnosis of localized empyema. There was, however, nothing in the past history suggesting pulmonary infection which might have had this sequela. In addition the disappearance of the shadow later and its reappearance with each attack of heart failure made this diagnosis seem unlikely. That it was due to fluid, accumulating during congestive heart failure, seemed then to be the most likely diagnosis. It did not seem justifiable at any time to aspirate the fluid for examination. The shadow first began to decrease in size coincident with an attack of precordial pain which was followed by fever. The two events appeared to be unassociated, though it was, of course, impossible to be certain of it. There was slight leucocytosis. During fever the patient had slight persistent cough and for this reason respiratory infection had to be considered.

X-ray photographs did not disclose evidence of bronchopneumonia. Bacteriological studies were also negative. In spite of the absence of pericardial friction rub and of changes in the electrocardiogram, a diagnosis of coronary occlusion was made. This was based on the history of cardiac pain, and the presence of fever and leucocytosis.

In the second and third admissions heart failure was not so severe as on the first; the shadow disappeared more quickly and without a rise in temperature, which occurred, as has already been said, coincident with its decrease in size during that admission. After observing the patient and the changes in the shadow on three occasions it was thought that the shadow could only have been cast by fluid, the presence of which was due to congestive heart failure. That it was fluid was definitely settled when the fourth attack of heart failure terminated fatally and the patient came to autopsy. The presence of fluid in the interlobar space and the obliteration of the right pleural cavity by adherence of the visceral and parietal layers of the pleura were, just as had been supposed, the pathological conditions. It was not possible to discover the underlying pathological process responsible for complete obliteration of the right pleural cavity. Why it occurred in this form rather than in the somewhat more common form of dense fibrous bands also cannot be explained. The patient did not recall having had an illness before the onset of the present one. The adhesion of the two layers of the pleura must already have occurred before the onset of the first attack of heart failure, since the shadow was discovered a few days after its onset.

Between the second and third admission the mechanism of the heart changed to auricular fibrillation. Because of enlargement of the heart, it seemed unwise to attempt to restore the normal rhythm with quinidine. After each attack of heart failure from which the patient recovered she found it necessary to lead life on a slightly lower level. At the time of the first admission the area of the heart (traced from x-ray photographs taken at a distance of 2 meters) measured 152.8 sq. cm., and on discharge 132.5 sq. cm., a decrease in size of 14 per cent having taken place. The maximum and the minimum sizes of the heart during this admission were 175.0 sq. cm. (February 4, 1927) and 130.0 sq. cm. (April 1, 1927) respectively. At the time of the second admission the area of the heart was 171.6 sq. cm., and on discharge, 144.4 sq. cm., that is to say a decrease of 16 per cent occurred. The heart remained, however, larger than it was at the time of the first discharge (132.5 sq. cm.). At the time of the third admission the area of the heart was 169.7 sq. cm., and on discharge, 148.4 sq. cm., a decrease of 13 per cent. The heart was again larger than it had been when the patient was discharged the first and second times. At the time of the fourth admission, March 6, 1928, the area was 157.8 sq. cm. and the smallest

recorded was 150.2 sq. cm. (April 4, 1928). In the last photograph taken on April 26, 1928, it was 160.8 sq. cm.

In studying the clinical course of the patient the rapidity with which the disease ran its course is striking. Before the first attack the patient had a few symptoms of congestive failure for six months, but afterward there were 4 attacks within eleven months. The last attack terminated fatally, fifteen months after onset and twenty-one months after the onest of the first cardiac symptoms. During fifteen months she was confined to hospital approximately six and a half months, and recovered satisfactorily from each of the first three attacks.

SUMMARY

A case is presented in which during each of 4 attacks of congestive heart failure a shadow was observed in x-ray photographs of the chest, the shadow seeming to occupy the space between the upper and middle lobes of the right lung. The shadow was thought to be cast by fluid, the amount being too small to give signs on physical examination. With disappearance of signs of heart failure the shadow also disappeared. The patient succumbed to the fourth attack of failure and autopsy examination revealed (as we had supposed it would) a small pleural effusion confined to the space between the upper and middle lobes of the right lung; adhesive pleurisy completely obliterating the remainder of the right pleural cavity. The etiology of the adhesive pleurisy was not discovered. The etiology of the heart disease was apparently primary atherosclerosis.

Department of Reviews and Abstracts

Selected Abstracts

Haberlandt, L.: Preparation and Demonstration of the Heart Hormone. Hdb. d. Biol. Arbeits meth., 1928, Section 5, Part 8, Heft 2, p. 237.

The author prepares his heart hormone by immersing the sinus venosus and great veins of two frogs (Rena Esculenta) in 1 c.c. of Ringer's solution. The extract may be equally obtained from the sinus node or the A-V bundle. When perfused through the isolated frog's ventricle by Straub's cannula, acceleration and increased amplitude of the beat will occur if the heart is hypo-dynamic or if it has stopped, pulsations will be initiated.

The extract employed differed from the accelerator material described by Loewi in not being destroyed by fluorescence or ultraviolet light. It does not resemble adrenalin as it produces vasodilation rather than vasoconstriction. The hormone may be extracted with alcohol, less easily with chloroform and not at all with ether. The aqueous extract seems to be the more suitable. The hormone is heat resistant and is adsorbed by charcoal.

Similar work done on warm blooded animals shows that an extract prepared in Locke's solution from the right auricle in dogs produced an increase in the number and amplitude of beats in rabbits' hearts.

The hormone does not seem to be genus specific and may be obtained from the entire conducting system of the heart. The author quotes the work of Ryland and De Moor, Kemal, Mouchet and others, who have worked on similar lines.

Cohn, Alfred E., and Stewart, Harold J.: The Relation Between Cardiac Size and Cardiac Output per Minute Following the Administration of Digitalis in Normal Dogs. Jour. Clin. Invest., 1928, vi, 53.

Following the administration of digitalis in normal dogs in so-called therapeutic amounts, the following effects were observed: the form of the T-wave in the electrocardiogram changed; cardiac output as determined by the principle of Fick was decreased; the size of the heart decreased, and the height of ventricular excursions increased. These excursions were determined by the authors' method of photographing the motion of points of the hearts' borders by casting shadows of these points made by roentgen rays upon moving films.

When digitalis was excreted all these measurements returned toward normal. The cardiac output often became greater than the initial value.

The authors conclude that digitalis within the first twenty-four hours decreases the output. The cardiac output which obtains at any later instant is the net result of the workings of two opposing factors. The first of these effects increases cardiac tone and results in decrease in the size of the heart. It is due to this action that cardiac output tends to decrease. The second effect increases ventricular contraction and tends to increase cardiac output. If cardiac size is not smaller than a critical value, increase in ventricular contraction overbalances decrease in size so that cardiac output increases beyond the beginning value.

Cohn, Alfred E. and Stewart, Harold J.: The Relation Between Cardiac Size and Cardiac Output per Minute Following the Administration of Digitalis in Dogs in Which the Heart is Enlarged. Jour. Clin. Invest., 1928, vi, 79.

The authors have studied the effect of digitalis upon the cardiac output, cardiac size and ventricular contraction of dogs with enlarged hearts, but without signs of heart failure.

The effect of digitalis on these hearts is the same whether they are normal in size or enlarged. They point out that it is still necessary to learn whether enlargement resulting from mechanical embarrassment requires differentiation from enlargement due to underlying disease in which edema is a conspicuous phenomenon.

Smith, W. Carter, Burwell, C. Sidney, and DeVite, Michael J.: The Effect of Atropine Upon the Output of the Hearts of Normal Men. Jour. Clin. Invest., 1928, vi, 237.

Atropine administered intravenously to normal men increases the rate of the heart relatively much more than the output of the heart per minute and thus produces a diminution in the output of the heart per beat. There is a relatively small rise in cardiac output per minute and no change in pulse pressure in metabolic rate following the use of the drug.

The absence of constant changes in the blood pressure levels indicates the extraordinary adjustability of a circulatory mechanism which can suffer a large sudden increase in pumping strokes per minute without alteration of pressure. Indeed it appears that heart rate, cardiac output, or blood pressure may change within limits, without involving each other, so perfect and instant are the compensatory mechanisms.

Burwell, C. Sidney, and Robinson, G. Canby: A Note on the Cardiac Output of a Single Individual Observed Over a Period of Five Years. Jour. Clin. Invest., 1928, vi, 247.

In 1924 the authors reported the results of a study of the output of the heart in normal resting adults and at that time noted that two of the subjects differed in the degree of variation exhibited by their cardiac output at different times but under identical circumstances. In one of the subjects five measurements scattered over a year varied only from 3700 to 3960 c.c. per minute.

The first group of measurements on this subject was made by the authors' method. Since that time a second series of determinations have been made by the method of Bock, Field, Gildea and Lathrop. The output of the heart remained relatively unchanged throughout the whole period. This general agreement constituted not only a demonstration of the degree of perfection of physiological regulation but also impressive evidence of the agreement in this subject of two quite different methods of measuring the output of the heart.

Markel, Albert G., and Pardee, Harold E. B.: The Correlation of Electrocardiographic and Necropsy Findings. Am. Jour. Med. Sc., 1928, clxxvi, 479.

The object of this investigation is an attempt to correlate the form of the ventricular waves of the electrocardiogram with the condition of the heart at necropsy. For this purpose, a study was made of a series of 10 cases in the wards of the New York Hospital. Two cases are presented with microscopically normal muscle and no significant abnormality of the electrocardiogram. Evidence is also presented that a curve showing notched QRS complexes with a slightly

abnormal duration and an abnormal T-wave represents the definite microscopic abnormality but one less severe than indicated by the curves of bundle-branch block or intraventricular block.

Birkhaug, Konrad E.: Allergic Reactions with a Toxin-Producing Strain of the Nonmethemoglobin-Forming Streptococcus Isolated from Rheumatic Fever. Jour. Infect. Dis., 1928, xliii, 280.

Guinea pigs and rabbits sensitized to the non-methemoglobin-forming streptococcus isolated from rheumatic fever may be rendered cutaneously hypersensitive to filtrates of cultures of this organism. A brief period of specificity in the sensitive state is recorded. This period is shortly followed by a sensitive state that is non-specific. During this phase of the cutaneous reactions, the allergenic property of the filtrate can be nullified completely with specific antiserums. After the end of the cutaneous allergy of this first phase, continued sensitization of the animals with living non-methemoglobin-forming streptococci produces the reappearance of cutaneous allergy. During the second phase, the reactions of allergy are nonspecific and the allergic principle of the filtrate is nonneutralizable with specific antiserums. For this phase, filtrates heated at 98° C. for four hours are not inactivated as allergic substances. Heterogeneity in the cutaneous responses of patients with rheumatic fever to filtrates of the non-methemoglobin-forming streptococcus and to certain strains of Streptococcus viridans might be explained on the basis of prolonged sensitization to any one dominant strain of the non-hemolytic streptococci. Desensitization of bacterially hyperallergic guinea pigs and rabbits was accomplished during the second phase of cutaneous allergy by intracardial or intravenous injections of bacterial filtrates.

Fischer, Robert: Clinical Studies of Paroxysmal Tachycardia and Parasystole. Wien. Arch. f. Klin. Med., 1928, xvi, 137.

In this paper an attempt was made to analyze two rare cases of tachycardia. In the first case of decompensated hypertension the paroxysmal tachycardia was caused by a reciprocal rhythm. Superventricular extrasystoles producing the attack caused a delay in conduction and a longitudinal dissociation in the His bundle allowing the normal impulse to return to the auricle from where a new impulse reaches the ventricle. Parasympathetic stimulation stopped this mechanism especially toward the end of the attack, so that longer periods of normal heart rhythm were present.

The second case showed a marked hypertrophy of the left ventricle and a certain number of extrasystoles alternated regularly with 2 normal systoles. The name "intermittierende tachycardie" was given to this condition. The case was analyzed according to the method of Kaufmann and Rothberger and the possible explanations for this phenomenon were discussed.

Blumgart, Herrmann L., and Weiss, Soma: Clinical Studies on the Velocity of Blood Flow. XI. The Pulmonary Circulation Time, the Minute Volume Blood Flow Through the Lungs, and the Quantity of Blood in the Lungs. Jour. Clin. Invest., 1928, vi, 103.

Measurements of both the minute volume flow through the lungs and the pulmonary circulation time have been made in 17 normal persons and the approximate amount of the blood in the lungs has been calculated. The average calculated amount of blood in the lungs was 984 c.c. or approximately 21 per cent of the total blood volume. The quantity varies considerably in different individuals.

The results indicate that the pulmonary circulation time is an index of the mean time consumed by the blood flow through the lungs.

The observations suggest that in normal persons the available pulmonary pathways are approximately equal.

Normal variations in the pulmonary circulation time are not related to corresponding normal variations in the minute volume blood flow through the lungs.

Chadwick, R. Taylor.: The Levulose Tolerance of Convalescent Children with Special Reference to Rheumatism. Arch. Dis. Childhood, 1928, iii, 179.

Levulose tolerance tests were done in a group of 35 children, 9 of whom were regarded as controls. The remaining 26 were rheumatic and were grouped according to the presence or absence of a heart lesion and according as to whether the process was active or quiescent.

The dose of levulose used varied between 20 to 30 gm. and the Hagedorn-Jensen method of estimating the blood sugar was used.

The control cases which were well showed either no change or a very slight rise in the blood sugar. The same occurred in cases of chorea who did not have cardiac involvement.

Levulose intolerance was demonstrable in cases of chorea with heart involvement and in acute rheumatic fever whether carditis was or was not present. With recovery the tolerance improved.

This intolerance is thought probably to be due to toxic absorption from a rheumatic focus.

Poynton, F. J., and Sheldon, W. P. H.: Coarctation of the Aorta with Ulcerative Aortitis. Arch. Dis. Childhood, 1928, iii, 191.

The authors report a case of coarctation of the adult type occurring in a boy of eight years. On examination a systolic murmur was audible loudest in the third and fourth intercostal spaces midway between sternal edge and right nipple; a large pulsating external mammary artery was present and blood culture showed a hemolytic streptococcus.

At autopsy the heart was slightly enlarged and the constriction in the aorta occurred just beyond the origin of the subclavian artery and beyond this an ulcer was present.

Other anomalies present included a bicuspid aortic valve and a common origin of the innominate and left common carotid arteries. The ductus arteriosus as in most cases of the adult form of the condition was closed.

The authors review 4 other cases of coarctation from the literature where an infectious aortitis was fatal.

Rosler, H.: Contributions to the Conception of Congenital Heart Disease. 1. X-ray Findings in Congenital Malformations of the Heart and the Vessels. Wien. Arch. f. Inn. Med., 1928, xxv, 487.

The author shows that positive x-ray findings were obtained in about 85 per cent of the 68 cases under his observation. In 50 per cent of these cases the x-ray picture was of definite value for the diagnosis of a malformation.

Rosler, H. L.: Contributions to the Conception of Congenital Heart Disease. 2. Investigation on the Etiology. Wien. Arch. f. Inn. Med., 1928, xxv, 495.

Sixty cases were followed up from this point of view. Thirty-two were male, 28 female. In none of these cases could a familial occurrence of congenital heart disease be found. In 7 cases there was positive evidence of rheumatic heart disease

in the family. Trauma, physical or mental disease of the parents during cohabitation or pregnancy did not contribute to the frequency of the malformations. The toxic effects of alcohol were thought responsible in 8 cases, but the amount of material was so small that the figures are within the limits of statistical error. The same was true for cases in which consanguinity of the parents was found. (6 cases.) A relation between congenital lues and congenital heart disease could not be established.

Rosler, H.: Contributions to the Conception of Congenital Heart Disease. 3. Observations on a Case of Pulmonary Stenosis. Wien. Arch. f. Inn. Med., 1928, xxv, 507.

The author gives an extensive report of the clinical, radiological and postmortem findings in a case in which the diagnosis had been made of pulmonary stenosis combined with defect of the interventricular septum. The autopsy showed that the stenosis of the pulmonary artery was caused by a diaphragm below the level of the valves with the remains of an old endocarditis. Other malformations present included congenital luxation of the hip and anomalous cervical vertebrae. An analysis of the discrepancies between clinical and autopsy observations was made.

Rosler, H.: Contributions to the Conception of Congenital Heart Disease. 4. Observations in Two Cases of Stenosis of the Isthmus of the Aorta. Wien. Arch. f. Inn. Med., 1928, xxv, 521.

Two typical cases of stenosis of the isthmus of the aorta, one of which could be confirmed by autopsy are described and the clinical radiological and anatomical picture of the condition is discussed.

Fleming, G. B., and Stevenson, Mary M.: Heart Block Associated with Congenital Malformation of the Heart. Arch. Dis. Childhood, 1928, iii, 221.

The authors report two cases of heart block associated with congenital malformation of the heart.

The first case was a male child of three and one-half years. The classical symptoms of congenital heart disease were not present but the heart was enlarged, a systolic murmur being audible over the precordium and transmitted to the axilla and right shoulder. The pulse varied between 30 and 60 and the electrocardiogram showed a complete and permanent auricular ventricular dissociation, the auricles beating between 80 and 125 and the ventricles between 35 and 50. The block was unaffected by atropine, adrenalin and exertion.

The second case is that of a girl eight years of age, who showed mental and physical retardation. Cyanosis, clubbing and polycythemia were present and fainting spells were frequent. The heart was enlarged. A systolic murmur was present over the precordium especially loud in the left third intercostal space and transmitted to the left third intercostal space and transmitted to the left clavicle and scapula. The "Q" wave was present. None of the measures attempted abolished the block but after exertion regular ectopic beats followed each normal beat, and during the compensatory pause, the blocked auricular beat was visible.

The authors discuss the pathology and state that the block per se causes little disability, any symptoms present being due to the presence of other anomalies.

Lampard, M. E.: Heart Block Associated with Congenital Heart Disease. Arch. Dis. Childhood, 1928, iii, 212.

The author reports a case of complete heart block in a boy of six years. The congenital nature of the lesion was surmised, although the author mentions the possibility of diphtheritic origin. The heart was enlarged and globular in shape, the ventricular rate being 48, the auricular 75. The blood pressure measured 116 systolic and 64 diastolic. A thrill and murmur were present over the pulmonic area and a diastolic bruit was later audible over the precordium. No clubbing, cyanosis or polycythemia were present.

The author summarizes the thirty cases reported in the literature and discusses the probable pathology of the condition. He concludes that the lesion is probably due, not so much to a hole in the ventricular septum but to the presence of fibrous tissue causing pressure on the His bundle. When the bundle runs on the edge of the septal defect it may be damaged by infectious processes.

White, Paul D.: The Effect of Strain on the Heart. New Eng. Jour. Med., 1928, excix, 801.

In a discussion of this important subject the author divides heart strain as due to intrinsic or extrinsic factors. The intrinsic factors consist of structural defects or lesions in the heart and disorders of rhythm. The extrinsic factors causing heart strain are of far less importance than the intrinsic ones with two exceptions. These exceptions are hypertension and hyperthyroidism.

These various points are discussed from a very conservative viewpoint and should prove of value in furthering our ideas as to what may be expected in an individual patient complaining of symptoms from his heart.

Ziskin, Thomas: The Electrocardiogram in Hypertension. Arch. Int. Med., 1928, xlii, 512.

A study was made of 100 consecutive patients with hypertension to determine the significance of electrocardiographic observations in hypertensive heart disease. Sixty-three of these patients showed some abnormality. These consisted of extrasystoles, delay in conduction, inversion in T-wave and evidence of left ventricular preponderance. The signs of left ventricular preponderance were present in only 44 of the 100 patients.

The author has investigated factors that determine the appearance of these signs of ventricular preponderance in patients with hypertensive heart disease.

Christian, Henry A.: Chronic Nonvalvular Disease of the Heart. Jour. Am. Med. Assn., 1928, xci, 549.

The author discusses chronic nonvalvular disease of the heart in contrast to chronic valvular heart disease in patients with symptoms of cardiac derangement in whom study does not reveal evidence of any lesions of the endocardium or pericardium. He points out that the myocardium is responsible in a great many patients for the symptoms of cardiac failure even though the muscle itself seems normally nourished and devoid of evidences of degeneration or inflammation.

Chronic myocardial insufficiency or chronic myocarditis is a very serious disabling disease of the heart and along with myocardial fatigue we find in this paper is the cause of cardiac symptoms in an extremely large proportion of cardiac patients.

This paper will be welcome to those physicians who find large numbers of patients of this type in their practice. Various features of this important condition are discussed.

Howard, C. P., and Mills, E. S.: Acute Articular Rheumatism and Other Members of the Rheumatic Cycle. Canad. Med. Assn. Jour., 1928, xix, 403.

The authors have studied a group of 241 patients admitted to the Montreal General Hospital for acute articular rheumatism or its complications during three years time. This group of patients represents 5 per cent of the total admissions during this time.

Arthritis occurred in 55.7 per cent under observation though there was a history of arthritis at some period of the disease in 80 per cent. Of the cardiac manifestations, there was an acute or chronic endocarditis in 68 per cent, myocarditis in 41 per cent and pericarditis in 17 per cent. Tonsillitis occurred in 46 per cent; acute or chronic pleurisy was surprisingly frequent, occurring in 15.3 per cent. The average hospital stay of the patient was six weeks. 20 per cent were discharged as cured, 64 per cent as improved and 5 per cent as unimproved. There was a mortality of 9 per cent.

Barr, David P.: Exercise in Cardiac Disease. Jour. Am. Med. Assn., 1928, xci, 1354.

The author emphasizes several principles which have a bearing on our conception of exercise in cardiac disease, reviewing the literature of our present knowledge.

In the study of muscular exertion two kinds of inadequacy must be considered separately. The first of these is a failure to supply the tissues with sufficient blood and oxygen. This may occur in any person at all, from the most highly trained athlete to the severely decompensated cardiac patient, but with different amounts of work. Whenever it occurs there is an oxygen debt, an accumulation of lactic acid and an exaggerated pulmonary response. Intrinsically it does not imply any abnormality, or cardiac weakness. The second form may be designated congestive heart failure and arises because the cardiac output does not keep pace with the inflow of blood to the heart. It is usually if not always dependent on myocardial insufficiency or disease. It occurs earlier and with less exertion when a mechanical factor, such as mitral stenosis, is also present.

In normal persons, exercise may be attempted in which sufficient supply of blood and oxygen to the tissues is impossible. Congestive cardiac failure, however, does not occur because respiratory factors limit the exercise before the maximum cardiac response has been attained. The patient with heart disease incurs an oxygen debt from more trivial causes. Dyspnea occurs earlier and is more severe. As in normal persons, the lungs may be the limiting factor and may protect the heart. The protection, however, may be insufficient and congestive heart failure may result.

In both normal persons and cardiac patients, dyspnea is the greatest safeguard against the possibility of heart strain and cardiac failure. Patients who have mechanical factors such as mitral stenosis have greater dyspnea and are more protected than those patients in whom this factor is absent. In patients with syphilitic disease of the aortic valve, with chronic hypertension and perhaps with myocardial defects, it may not be safe to accept dyspnea as the warning signal for the control of exercise. The observance of other symptoms or, indeed, an entirely arbitrary limitation of exertion may be necessary to furnish sufficient protection.

Levine, Samuel A., Fulton, Marshall N.: The Relation of Hypertension to Mitral Stenosis. Am. Jour. Med. Sc., 1928, clxxvi, 465.

To confirm an impression that patients with mitral stenosis over the age of forty-five years commonly have an elevated blood pressure, the authors have studied 762 cases of mitral stenosis admitted to the wards of the Peter Bent Brigham

Hospital, between 1913 and 1927 and those seen in private practice during the past eight years. The cases have been divided arbitrarily according to age, as those over or under forty-five years. As those with hypertension, all cases having a systolic pressure of 105 mm. or over and a diastolic of 90 mm. or over have been included. Only those cases have been included in which the mitral valve alone was involved. Only cases were included in the hypertensive group in which the physical findings during life were sufficient to make a diagnosis of mitral stenosis quite certain.

Of the total of 762 cases, 159, 21 per cent were over forty-five years of age. Only 17 of these were examined after death. They all showed definite mitral stenosis, some with a mere crescentic slit, others with a less marked degree.

The study of these cases seems to indicate that with advancing years patients with mitral stenosis have vascular hypertension with much greater frequency than the average population. Out of 159 cases there were 92 or 58 per cent with hypertension. Mitral stenosis of itself tends to have a blood pressure slightly lower than normal. Evidence is presented from the study that the mitral stenosis found in older patients is not a part of the general sclerotic process alone, but must be rheumatic in origin in as much as these patients have the same incidence of a previous history of rheumatic fever or chorea as do the younger patients.

The authors feel the unusual association of hypertension with mitral stenosis results from a particular vulnerability that these patients have both for the infectious and degenerative types of vascular disease.

There is some evidence from this study to show that vascular hypertension exercises a beneficial effect on cases of mitral stenosis. This can be explained on the basis that the increased load on the left ventricle as a result of the hypertension tends to keep this cavity dilated and to stretch the mitral ring and thereby to delay the contraction resulting from the mitral stenosis. It also tends to obviate the imbalance of the two ventricles.

Schneier, Joseph: The Indications for Tonsillectomy in Arthritis and So-called Rheumatic Diseases. Wien. Arch. f. Klin. Med., 1928, xvi, 119.

In 39 cases of acute rheumatic fever in adults followed over a period of from two to sixteen years after tonsillectomy, 31 were cured. In secondary chronic arthritis (arthritis and myalgia following acute rheumatic fever) out of 43 cases, 18 were cured, 10 improved and 15 did not show improvement. In all the other forms of "so-called" rheumatic disease tonsillectomy did not improve the condition.

The author proposes to do a tonsillectomy after the acute stage in acute rheumatic fever and in secondary chronic arthritis independent of the clinical appearance of the tonsils.

Farnum, Waldo B.: The Effect of Tonsillectomy on Existing Cardiac Disease in Adults. Am. Jour. of Med. Sc., 1928, clxxvi, 474.

This study has particularly to do with the results of tonsillectomy on a preexisting endocarditis. The cases used for the investigation were 526 patients followed in the adult cardiac clinic at St. Luke's Hospital, New York for from two weeks to nine years. The author concludes that tonsillectomy although carried out under as nearly ideal conditions as may be obtained may initiate an attack of acute rheumatic polyarthritis in a certain number of cases, and further an actual spread of endocardial or myocardial infection.

The recurrence of sore throat may not be avoided since infection elsewhere in the nasopharynx may recur. With these recurrences, there may be oftentimes attacks of acute rheumatic polyarthritis and renewed cardiac involvement. Tonsillectomy

in this group of cases does not seem to have a very great effect on the recurrence of chorea, as about 20 per cent recurred in both the tonsillectomized and the non-tonsillectomized.

It seems fair to conclude from these observations that in adults with existing cardiac disease the hope for improvement placed in tonsillectomy has not been certain. If tonsillectomy is to be generally used in the future as a definite therapeutic measure in cardiac disease, its best result will be obtained before the incidence of heart infection or very early in its course.

The author points out that carditis is but one phase of a generalized infection spoken of as rheumatic fever. The tonsils may, or may not, be the existing focus which keeps up this infection. If the tonsillectomy is accomplished after the onset of carditis it will not necessarily prevent further recurrences because the cause of the infection may still be present in the throat or elsewhere in the body. The preventive treatment should be based on the raising of the individual's resistance to infection by all possible means.

Freund, Ernst: Rheumatic Nodules in Chronic Polyarthritis. Wien. Arch. f. Klin. Med., 1928, xxvi, 73.

Discussing the clinical and anatomical appearance of rheumatic nodules in acute rheumatic fever and primary chronic arthritis with their numerous analogies the author feels that we are not able to determine the etiology of both diseases.

The anatomical and bacteriological study of six cases of chronic arthritis showed certain analogies anatomically with the subcutaneous nodules of rheumatic fever but the author was unable to isolate any organisms.

His findings are therefore inconclusive in determining whether both diseases have a similar etiology.

Bourne, Geoffrey: Notes on a Case of Heart Block Whose Grade was Decreased by an Inspiratory Increase in Sympathetic Tone. St. Barts. Hosp. Reports, 1928, lxi, 146.

The author reports a case of 2:1 heart block occurring in a woman with exophthalmic goitre. On observation, it was noted that an inspiratory decrease in the block occurred and that for a few beats a 1:1 rhythm was present.

To discover whether this phenomenon was due to vagal inhibition, sympathetic stimulation or the result of increased heart filling various tests were tried.

The influence of the vagus was investigated by giving atropine and pilocarpine. With the former drug the respiratory reflex was more pronounced, with the latter, it was abolished, but no decrease in the amount of the block was observed. Ocular and vagal pressure was ineffective. The effect of stimulation of the sympathetic was investigated by noting the effect of adrenalin, exercise and psychical excitement. It was found that adrenalin temporarily abolished the block and that emotion seemed to have a similar transient effect. Exercise did not change the inspiratory block-decreasing effect. No effect on the degree of block was obtained when the heart was overfilled by pressure on the patient's abdomen. The respiratory reflex remained.

The author concludes that the respiratory effect is due to an increase in the sympathetic tone occurring during inspiration.

Bourne, Geoffrey: The Treatment of Rheumatic Carditis. The Lancet, August 4, 1928, 217.

The author summarizes the physical signs of active cardiac infection in rheumatic children. He emphasizes the need for prolonged bed rest, in such cases. The tonsils if diseased are removed. The criteria of tonsillar disease include the history of sore

throats, the presence of cervical lymphadenitis and the appearance of the tonsils themselves. The dangers of tonsillectomy during the active stages of the disease are stressed.

Salicylates by mouth and a gargle of potassium permanganate are recommended. No encouraging results have been obtained from the use of vaccines, from intravenous disinfectants or from artificial sunlight.

Wiechowski, W.: Treatment of Cardiac Syncope. Wien. Klin. Wchnschr., 1928, xli, 475.

The author discusses the different forms of cardiac syncope due to injury to the heart, peripheral circulation or nervous system. He reviews briefly the methods which have been employed to test the effect of drugs on the circulatory system. According to Wiechowski, the effect of drugs can best be judged from their effect on the minute volume. He and his coworkers have investigated the following substances: camphor, digitalis, caffein, adrenalin and three new drugs with an effect analogous to camphor: Kardiazol, Coranin and Hexeton. The results of this work have already been published. Caffeine and adrenalin alone are reliable in producing an increase in the normal minute volume of the heart. In agreement with the findings of Winterberg and American investigators camphor has very little direct effect on the heart and the vasomotor center, while the three drugs mentioned above stimulate the vasomotor center. Indirectly, camphor excreted in the lungs may produce here a dilatation of the vessels and the bronchioles and may thus have an indirect action on the heart.

For the practitioner caffein should be the drug used in all kinds of circulatory collapse both for its direct effect on the minute volume and for its dilatation of the peripheral vessels. After the heart has stopped beating, intracardial injection of caffeine is indicated. The use of adrenalin is limited because it forces a weakened heart to work against a peripheral vaso-constriction and increased blood pressure.

Musser, J. H.: Theophylline-Ethylenediamine in Heart Disease Associated with Pain. Jour. Am. Med. Assn., 1928, xci, 1242.

The abstracted histories of 20 patients with several types of heart pain are indicative of the therapeutic effect of theophylline-ethylenediamine. The greatest value of the drug lies in the treatment of patients with angina pectoris. It is only slightly less valuable in the handling of patients who have survived the initial effect of coronary thrombosis.

The author points out that rest in bed, diet and proper fluid intake alone will be sufficient in many cardiac patients to restore compensation. However, it definitely seems that patients with comparable signs and symptoms of cardiac failure of a congested type improve more rapidly and more fully with digitalis therapy combined with rest in bed and theophylline-ethylenediamine than they do under the same regimen without theophylline-ethylenediamine.

Smith, Fred M.: The Diet and Theophylline in the Treatment of Cardiac Failure. Jour. Am. Med. Assn., 1928, xci, 1274.

Further observations on the diet previously reported have emphasized the importance of this feature in the treatment of cardiac failure.

A greater significance is attributed to the carbohydrates and particularly the sugars of the diet. The beneficial action of carbohydrates on the liver injury induced by prolonged congestive failure may contribute to the effectiveness of the diet.

Intravenous administration of dextrose solution is not advocated if the patient is able to take food by mouth. It is felt that the diet is a more effective means of providing sugar.

Theophylline is a valuable measure in the treatment of the cardiac failure of arteriosclerosis. The best results are obtained in the congestive type of failure. Experimental and clinical observations support the belief that the elimination of fluid is promoted by the favorable influence on the coronary circulation.

Lukens, F. D. W.: Tolysin in Subacute Rheumatic Carditis. Jour. Clin. Invest., 1928, vi, 319.

In order to determine the effect of tolysin on subacute rheumatic carditis, the author selected 6 children with rheumatic heart disease in whom the joint symptoms were minimal and the carditis the most prominent feature. The diagnosis in all these cases was rheumatic heart disease, active, with mitral stenosis and insufficiency and enlargement of the heart. There were no arrhythmias and although the lesions were fairly severe, none of these patients showed failure of compensation. The pulse rate was not affected by treatment in any of these patients.

The absence of any demonstrable effect of tolysin upon the weight, temperature and leucocytosis in this type of rheumatic heart disease is evident from the data published in the tables.

Graham, Stanley: Arsenic in the Treatment of Chorea. Arch. Dis. Childhood, 1928, iii, 206.

The author surveys the results of 3 forms of therapy used in 3 groups of children suffering from chorea. One group was treated with intravenous neokharsivan an average of 0.465 gm. arsenic being given per patient during thirty days. A second group was given liquor arsenicalis (liquor potassii arsenitis), the average amount of arsenic given being 0.276 gm. or about half the amount administered to the first group. A third series was treated with sodium salicylate.

The series of patients was further subdivided according to the length of time chorea had been present before treatment. The duration of the chorea in days subsequent to treatment and the condition of the heart on admission and discharge was taken as the criteria of the efficacy of the drug.

As far as the duration of the disease was concerned, the group treated with salicylates improved the quickest, and those treated with intravenous arsenic most slowly.

The heart murmurs cleared more in the group treated with Fowler's solution than in the other two.

The author concludes that drug therapy is of little value in chorea, that improvement is due to the tonic effect of the arsenic and is not proportional to the amount given. General measures are recommended and the use of sodium salicylate for its action on rheumatic manifestations.

Turner, Roy H.: A Sphygmograph Using a Carbon Grain Microphone and the String Galvanometer. Bull. Johns Hopkins Hosp., 1928, xliii, 1.

A sphygmograph for clinical and experimental purposes using the string galvanometer as a recording instrument is described and its possibilities indicated.

A carbon grain microphone mounted over the vessel through variation in pressure causes the current passing through to pulsate. These current pulsations are recorded by photographing the shadow of the galvanometer string.

The microphone functions largely as a result of pressure changes rather than movement of parts. The instrument is without demonstrable lag.

Records show a form agreeing with accepted standards, and exhibit accuracy of the time element.

Turner, Roy H.: A Method for Measuring the Velocity of the Pulse Wave in which Helium Glow Lamps are Used as Markers. Bull. Johns Hopkins Hosp., 1928, xliii, 14.

An instrument and method for measuring the velocity of the pulse wave is described. The flashes of helium-filled glow lamps photographed on the moving film serve to indicate the time of arrival of the pulse under carbon grain microphones.

The instrument is without demonstrable lag.

The beginning of the flash may be made to coincide with the beginning of the upstroke of the sphygmogram.

Detailed data for determination of pulse wave velocity in six subjects are presented.

Marvin, H. M.: The Heart During Anesthesia and Operative Procedures. New Eng. Jour. Med., 1928, cxcix, 547.

The author discusses this important subject from the standpoint of general anesthesia procedure by ether, ethylene and nitrous oxide gas. He presupposes that chloroform produces definite injury to the heart and that in the hands of inexperienced anesthetists any anesthetic may injure the patient at this time.

He believes there is no convincing evidence that anesthesia and operation in themselves have any damaging action upon the normal heart. The damaged heart whatever its physical signs is the equivalent of a normal one for anesthesia and operation if it is carrying on an adequate circulation under normal conditions of life with a possible exception of the syphilitic heart; no matter what size the heart may be, no matter what thrills or murmurs may be present over the precordium, no matter how far nor in what direction sounds or murmurs may be transmitted if the patient has been leading the life involving moderate activity and has been without symptoms it may be safely assumed that it will behave properly during anesthesia and operation. There are three types of heart disease that are notoriously apt to lead to sudden death, even at complete rest: syphilitic heart disease with aortic insufficiency, complete heart block as a manifestation of any type of heart disease and that form of heart failure known as angina pectoris. The history, therefore is more important than the physical examination although both should be obtained.

Patients with heart failure and those of auricular fibrillation even without heart failure should receive digitalis before operation if possible. The digitalis should be given in therapeutic doses or not at all and it should not be given as a routine preoperative measure.

Of the available general anesthetics, ethylene gas is probably the one that has the most to commend it, for use in patients with heart failure; and finally possibly most important of all it is more important to select the proper anesthetist than to select the anesthetic.

Book Reviews

Harvey, William: EXERCITATIO ANATOMICA DE MOTU CORDIS ET SANGUINIS IN ANIMALIBUS, With an English Translation and Annotations by Chauncey D. Leake. Charles C. Thomas, Publisher, Springfield, Illinois, 1928.

This book is published as a tercentennial edition of the original book by Harvey. Part I consists of a facsimile of the Latin edition reproduced by a new and exceedingly accurate process in photo-engraving. Part II is the English translation made by the author. This translation is based on the Longhine edition of 1697. Willis' translation of the dedication has been included since this is missing from the Longhine edition. The translator has also made use of a copy of Moreton's privately printed facsimile of the original edition. From these two sources, the author has prepared his own translation. He states that he has made this admittedly free in a deliberate attempt to present Harvey's thoughts in the current physiological manner. Thus while Harvey nowhere uses a word which may be literally rendered "pump" the author prefers to refer to cardiac action in some such term.

In order to bring out the significance of Harvey's work in regard to our modern knowledge of cardiac function, and to relate it to the slow development of this knowledge footnotes have been added to the translation.

This volume in connection with others which have appeared this year as part of the tercentennial celebration of the appearance of Harvey's great book should appeal strongly to students of Physiology and also to those interested in Medical history. A chronology of the life of William Harvey has been added.

There are included 10 illustrations, chiefly reproductions of the well-known Harverian pictures. These have been carefully collected from well-known sources and are presented in this volume in excellent form. They add greatly to the value of the book.

The book was set, printed and bound by the Collegiate Press, Menasha, Wisconsin. The cover design and front matter have been prepared and set with great care. The type face of the English translation is the very beautiful Caslon Old Style No. 337. It was designed by William Caslon, an engraver, in the early eighteenth century. Its characteristic is that of simple, honest design and perfect craftsmanship. The paper is eighty pound Natural Laid Aurelian Book.

The author has selected the material carefully and has rendered an excellent translation, avoiding all stilted and involved terms. The reading of this translation is easy and fascinating. It marks a distinct advance in publication of medical historical volumes.

The publishers are to be congratulated on the fineness of form and great attention to interesting and professional details.

CRITERIA FOR THE CLASSIFICATION AND DIAGNOSIS OF HEART DISEASE. By a Committee (Joseph H. Bainton, M.D., Robert L. Levy, M.D., W. C. Munly, M.D., M.C., U.S.A., and Harold E. B. Pardee, M.D., Chairman) Appointed by the Heart Committee of the New York Tuberculosis and Health Association, Inc., New York, Paul B. Hoeber, Inc., 1928, pp. 92.

The Heart Committee of the New York Tuberculosis and Health Association has devoted a great deal of attention to raising the standards of cardiac diagnosis, not only in the larger centers where the more elaborate methods of study are available, but in every Heart Clinic, no matter how small. The Committee believes that a complete and accurate diagnosis, including etiology, pathological anatomy, physiology and functional capacity, is of the greatest importance, and that a diagnosis made in one city should mean the same thing in any other city. In this little volume of 92 pages the Committee has brought together a commentary on the Nomenclature for Cardiac Diagnosis approved by the American Heart Association. This commentary takes up each heading, discussing it and defining the terms, and makes it possible for workers in all parts of the country to use the Nomenclature in a uniform manner. The discussion is practical and special emphasis is laid on methods of examination which are within the reach of everyone. With the aid of this book a complete cardiac diagnosis should be within the reach of every physician, and records from clinics in all parts of the country should be comparable for statistical studies in a manner not possible heretofore. The section on Etiology offers many valuable suggestions, perhaps the most valuable being the emphasis on the point that the correct etiological diagnosis is often "unknown." The sections on Anatomy, Physiology and Functional Capacity should be of general interest. There are suggestions for making an examination and a table of terms to be used in describing heart sounds and murmurs. Adherence to these systematic methods of examining and describing would result in reliable and easily interpreted records. Functional capacity is tested by the patient's ability to perform physical activity, not by arbitrary tests, and it is important to note that the functional classification depends solely on this ability and is not to be influenced by the anatomical prognosis or the prognosis. The term "Fibrosis of the Myocardium" is added to the headings.

A few points raise a question in the mind of the reader. The relation of hypertension to arteriosclerosis seems dogmatic; the diagnosis of tumor of the heart and of adherent pericardium seems almost too easy; and the discussion of "potential" and "possible" heart disease is rather brief. On the whole the style is as clear as it is concise, and the criteria are those which can be determined and used by all workers. There is now no excuse for incomplete or inaccurate records.